Supporting info

for

LiTMP-LiBr Complex-Induced Lateral Lithiation and Cross Ester Condensation: Direct Access to Isocoumarins from 2-methoxy o-Toluate Esters

Mintu Rehman, Sajib Daimary, Rasajna Madhusudhana, Rajendar Goreti*

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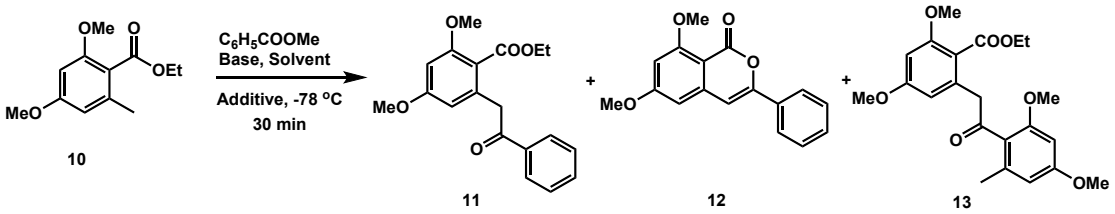
General Techniques: All the reactions utilizing air- or moisture sensitive reagents were performed under an atmosphere of argon and nitrogen in flame dried glassware. Tetrahydrofuran (THF) was double distilled from LAH, Dichloromethane (DCM) was distilled from CaH_2 before use. Commercially available reagents were used as received. Silicon oil bath was used for reactions that required heating. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm silica gel glass plates (60-F_{254}) that were analyzed by fluorescence upon 254 nm irradiation or by staining with p-anisaldeyde/AcOH/H_2SO_4/EtOH or by staining with $KMnO_4$ solution. The products were purified by column chromatography on silica gel (spherical, neutral, 100−230 μm) with an eluent of Pet-ether/EtOAc. NMR spectra were recorded with Avance III-500 (Bruker) (^{1}H: 500 MHz, ^{13}C: 125 MHz) spectrometer and referenced to the solvent peak at 7.26 ppm (^{1}H), 77.00 ppm (^{13}C) for $CDCl_3$ and 96.16 ppm (^{13}C) for CCl_4. Infrared spectra were recorded with a Bruker-Alpha (ATR-ZnSe) spectrometer and reported as wavenumber (cm^{-1}). A Q-Exactive benchtop HRMS was used for the high-resolution analysis.

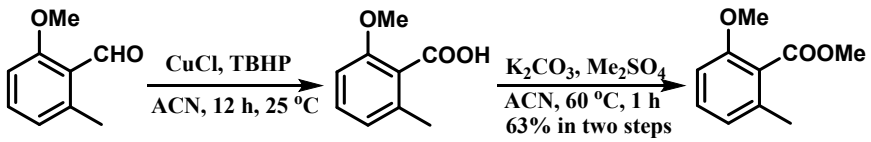
Optimization of reaction conditions:



Entry	Base(eq)	Additive (eq)	Reaction condition	Solvent	Yield (%)[c]			
					11	12	13	10
1	LDA (1.5)	LiI (10)	Condition B	THF	-	-	-	-[a]
			Condition A	THF	-	-	-	
2	LDA (3)	$LiClO_4$ (10)	Condition B	THF	-	-	-	-[a]
3[b]	LDA (5)	LiI (10)	Condition B	THF	-	-	-	-[a]
			Condition A	THF	-	-	-	
4[b]	LDA (1.5)	LiCl (10)	Condition B	THF	18	24	12	40
			Condition A	THF	-	-	-	-
5	LHMDS (5)	LiBr (3)	Condition A	THF	-	-	-	100
6[b]	$Li(NCy)_2$ (5)	LiBr (3)	Condition A	THF:Hexane (2:1)	-	28	-	-
7	LiTMP (5)	LiBr (3)	Condition A	THF:Toluene (2:1)	-	33	-	-

Table 1: [a] decomposed starting material. [b] The reactions were conducted for a duration of 2 h, but the results were same as 30 min. Condition A: Base was added to the solution of **10**, methyl benzoate and LiBr mixture in THF at -78 °C. Conditions B: Methyl benzoate was added to the preprepared enolate of **10** at -78 °C. [c]isolated yields.

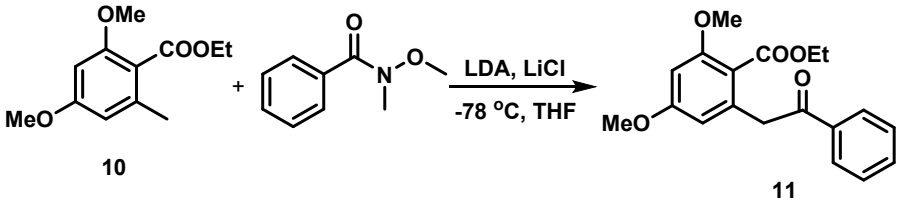
Experimental Procedures:



Preparation of methyl 2-methoxy-6-methylbenzoate (6): To a stirred suspension of aldehyde **6a** (1.5 g, 9.99 mmol) and CuCl (0.5 g, 0.5 mmol) in acetonitrile (20 mL), was added TBHP (70% in H_2O, 1.42 mL, 9.99 mmol) dropwise. The reaction mixture was

allowed to stir at room temperature for 12 hr. The reaction mixture was basified using sat. $NaHCO_3$ until pH 8.0-8.5 and extracted with EtOAc. The aqueous layer was acidified to pH2 using 2N HCl and extracted with EtOAc (3 x 20 mL). The combined organic layer was washed with water, brine solution, dried over Na_2SO_4 and the crude **6b** was used directly for next step.[4]

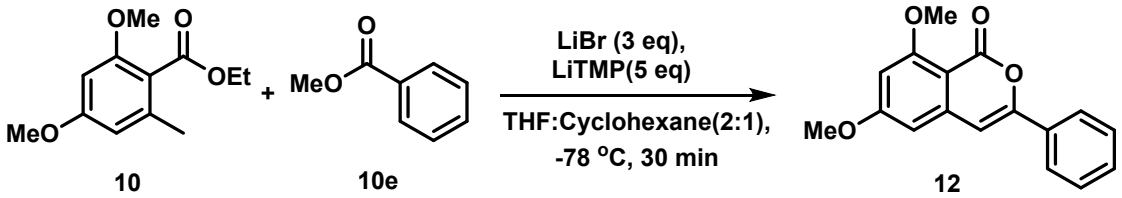
To a stirred suspension of crude acid **6b** (1.2 g) and K_2CO_3 (6 g, 45 mmol) in acetonitrile (30 mL), was added Me_2SO_4 (4.2 mL, 45 mmol). The reaction mixture was heated at 60 °C for 1 hr. The completion of the reaction was confirmed by TLC analysis. After cooling, the reaction mixture was added water (50 mL), extracted with EtOAc (25 mL x 3). The combined organic layer was dried over anhydrous Na_2SO_4, concentrated under vacuum and purified by column chromatography (silica gel, petroleum ether:EtOAc = 7:1) to obtain the corresponding ester **6** (1.13 g, 63% in overall two steps) as yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18-7.15 (t, *J* = 16, 8 Hz, 1H), 6.73-6.72 (d, *J* = 7.5 Hz, 1H), 6.69-6.68 (d, *J* = 8.5 Hz, 1H), 3.84 (s, 3H), 3.74 (s, 3H), 2.21 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 168.8, 156.3, 136.4, 130.3, 123.6, 122.3, 108.4, 55.8, 52.2, 19.2. IR (neat, cm^{-1}) 2970, 1735, 1609, 1463, 1324, 1252, 1210, 1145. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{10}H_{12}O_3$ 181.0870; Found 181.0878.



Ethyl 2,4-dimethoxy-6-(2-oxo-2-phenylethyl)benzoate, (11):[1] To a stirred solution LDA (2 M in THF, 0.645 mL, 1.2 mmol) and LiCl (0.97 g, 23 mmol) in dry THF (10 mL) at -78 °C under nitrogen atmosphere was added solution of ester **10** (0.515 g, 2.3 mmol) in THF (5 mL) dropwise over 5 minutes. After 45 min, to the deep red colour solution was added Wienreb`s amide (0.56 mg, 2.76 mmol) in THF (5 mL), stirred for 12 hours at the same temperature. Completion of the reaction was confirmed by TLC analysis. The reaction mixture was treated with 1N HCl (5 mL) at -78 °C, warmed to room temperature, and the aqueous solution was extracted with ether (3 x10 mL). The combined organic layer was washed with water, brine solution, dried over anhydrous Na_2SO_4, filtered and concentrated

under reduced pressure. The crude product was purified by column chromatography (silica gel,10% EtOAc/Pet ether) to obtain compound **11** (0.398 g, 71%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01-8.00 (d, *J* = 8 Hz, 2H), 7.57-7.54 (t, *J* = 14.5, 7 Hz, 1H), 7.47-7.44 (t, *J* = 15, 7.5 Hz, 2H), 6.41 (s, 1H), 6.35 (s, 1H), 4.33 (s, 2H), 4.24-4.20 (q, *J* = 14.5, 7 Hz, 2H), 3.81 (s, 3H), 3.78 (s, 3H), 1.20-1.17 (t, *J* = 14.5, 7 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 196.6, 167.7, 161.7, 159.1, 136.7, 135.7, 133.2, 128.7, 128.4, 116.5, 107.4, 97.8, 61.0, 56.0, 55.4, 43.8, 14.1. IR (neat, cm^{-1}) 2924, 1740, 1607, 1462, 1377, 1277, 1163. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{19}H_{20}O_5$ 329.1383; Found 32 9.1384.

Preparation of 3-substituted isocoumarin: General procedure: -

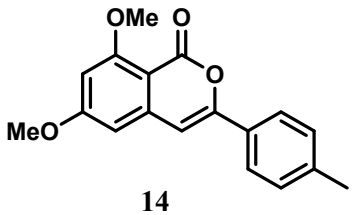


Conditions A: To a stirred solution of LiBr (0.230 g, 2.67 mmol) in THF:Cyclohexane (15 mL, 2:1) was added ortho-tolyl ester **10** (0.200 g, 0.89 mmol) and methyl benzoate (0.121 g, 0.89 mmol). The reaction mixture was allowed to stir at rt for 15 min. The reaction mixture was then brought to -78 °C and freshly prepared LiTMP (4.9 mmol, in THF) was added dropwise at -78 °C, until red coloured solution persisting, indicating the generation of orcillinate anion. After stirring for 30 min, the completion of the reaction was confirmed by TLC analysis. The reaction mixture was then treated with saturated aqueous NH_4Cl (10 ml), the organic layer was separated. The aqueous layer was extracted with EtOAc (20 mL x 2), the combined organic layers were washed with water, brine, dried over $NaSO_4$, filtered and the solvents were removed under reduced pressure. The crude product was purified by column chromatography (silica gel, 50% EtOAc/Pet ether) to obtain the desired isocoumarin **12 (**0.231 g, 92%**)** as yellow oil.

Scale up reaction: Compound **10** on 1.2 g provided product **12** in 1.35 g, 90% yield.

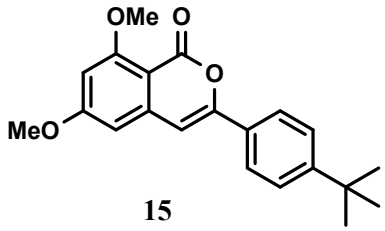
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73-7.71 (dd, *J* = 8, 1.5 Hz, 2H), 7.33-7.27 (m, 3 H), 6.61 (s, 1H), 6.29-6.27 (dd, *J* = 9.5,2 Hz, 2H), 3.85 (s, 3H), 3.78 (s, 3H); ^{13}C{^{1}H} NMR (125

MHz, $CDCl_3$) δ 165.2, 163.1, 158.2, 154.1, 142.0, 131.8, 129.8, 128.6, 125.2, 103.3, 101.6, 100.3, 98.6, 56.0, 55.4; IR (neat, cm^{-1}) 2953, 1730, 1605, 1463, 1373, 1223. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{17}H_{14}O_4$ 283.0965; Found 283.0956. Melting point 163-164 °C.



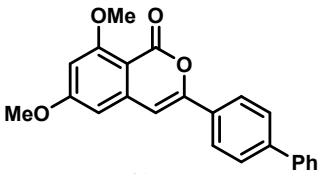
14

6,8-dimethoxy-3-(p-tolyl)-1H-isochromen-1-one, (14):[8] Conditions A was followed for the synthesis of the isocoumarin **14**. The product **14** was obtained as white solid (0.128 g, 91%).^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76-7.74 (d, *J* = 8.5 Hz, 2H), 7.23-7.22 (d, *J* = 8 Hz, 2H), 6.71 (s, 1H), 6.41 (s, 2H), 3.98 (s, 3H), 3.91 (s, 3H), 2.40 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) 165.2, 163.3, 158.5, 154.6, 142.4, 140.0, 129.4, 125.3, 103.4, 101.0, 100.1, 98.6, 56.2, 55.5, 21.5. IR (neat, cm^{-1}) 2941, 1724, 1605, 1463, 1373, 1221, 1166, 1060. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{18}H_{16}O_4$ 359.1278; Found 359.1272. Melting point 163-165 °C.



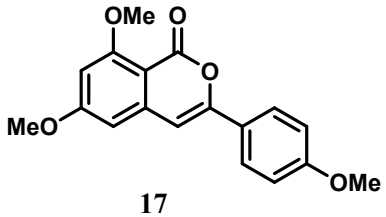
15

3-(4-(tert-butyl)phenyl)-6,8-dimethoxy-1H-isochromen-1-one, (15): Conditions A was followed for the synthesis of the isocoumarin **15**. The product **15** was obtained as pale-yellow liquid (0.138 g, 86%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64-7.63 (d, *J* = 8.5 Hz, 2H), 7.31-7.29 (d, *J* = 8.5 Hz, 2H), 6.56 (s, 1H), 6.26 (s, 1H), 6.23 (s, 1H), 3.81 (s, 3H), 3.75 (s, 3H), 1.24 (s, 9H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) 165.0, 163.0, 158.2, 154.1, 152.9, 142.1, 128.9, 125.4, 124.9, 103.0, 100.9, 100.0, 98.3, 55.8, 55.3, 34.6, 31.1. IR (neat, cm^{-1}) 2978, 1727, 1604, 1572, 1370, 1222, 1166, 1132. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ calc. for $C_{21}H_{22}O_4$ 339.1591; found 339.1590.



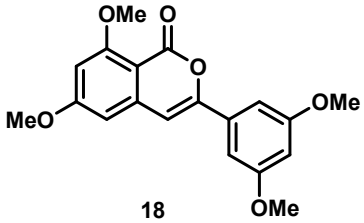
16

3-([1,1'-biphenyl]-4-yl)-6,8-dimethoxy-1H-isochromen-1-one, (16): Conditions A was followed for the synthesis of the isocoumarin **16**. The product **16** was obtained as white solid (0.155 g, 91%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89-7.88 (d, *J* = 8.5 Hz, 2H), 7.63-7.58 (m, 4H), 7.44-7.41 (t, *J* = 15,7 Hz, 2H), 7.36-7.33 (t, *J* = 14.5,7 Hz, 1H), 6.76 (s, 1H), 6.41-6.39 (dd, *J* = 11.5,2 Hz, 2H), 3.95 (s, 3H), 3.89 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) 165.3, 163.3, 154.0, 142.6, 142.2, 140.1, 130.7, 128.9, 127.8, 127.3, 127.0, 125.7, 103.4, 101.7, 100.3, 98.7, 56.1, 55.5. IR (neat, cm^{-1}) 2943, 1731, 1605, 1466, 1223, 1134, 1001. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{23}H_{18}O_4$ 359.1278; Found 359.1272. Melting point 162-164 °C.



17

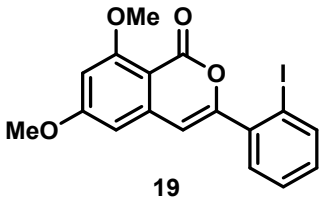
6,8-dimethoxy-3-(4-methoxyphenyl)-1H-isochromen-1-one, (17):[9] Conditions A was followed for the synthesis of the isocoumarin **17**. The product **17** was obtained as white solid (0.139 g, 94%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77-7.75 (d, *J* = 9 Hz, 2H), 6.90-6.89 (d, *J* = 9 Hz, 2H), 6.59 (s, 1H), 6.36 (s, 2H), 3.95 (s, 3H), 3.88 (s, 3H), 3.84 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) 165.2, 163.3, 161.1, 158.4, 154.4, 142.6, 126.9, 124.5, 114.1, 103.2, 100.1, 99.9, 98.3, 56.1, 55.4, 55.2. IR (neat, cm^{-1}) 2948, 1732, 1605, 1521, 1468, 1262, 1167. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{18}H_{16}O_5$ 313.1071; Found 313.1066. Melting point 146-148 °C.



18

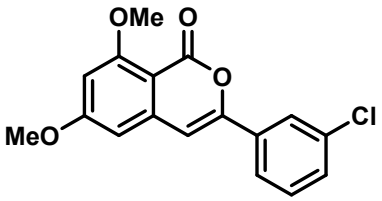
3-(3,5-dimethoxyphenyl)-6,8-dimethoxy-1H-isochromen-1-one, (18): Conditions A was followed for the synthesis of the isocoumarin **18**. The product **18** was obtained as pale yellow solid (0.136 g, 84%) ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.97-6.96 (d, *J* = 2 Hz, 2H), 6.73 (s, 1H), 6.49-6.48 (t, *J* = 4.5, 2 Hz, 1H), 6.43 (s, 2H), 3.97 (s, 3H), 3.91 (s, 3H), 3.85 (s, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) 165.4, 163.3, 161.0, 158.6, 154.2, 142.1, 133.9, 103.4, 102.5, 102.3, 100.4, 56.3, 55.6; IR (neat, cm^{-1}) 2946, 1734, 1605, 1467, 1371, 1214, 912. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{19}H_{18}O_6$ 343.1176; Found 343.1161. Melting point 218-220 °C.

Preparation of 3-(2-iodophenyl)-6,8-dimethoxy-1H-isochromen-1-one, (19): Conditions B: To a stirred solution of LiBr (0.232 g, 2.67 mmol) and ortho-tolyl ester **10** (0.89 mmol) in THF:Cyclohexane (2:1) was added freshly generated LiTMP (4.45 mmol, in THF) dropwise at -78 °C. To the red coloured solution (orcillinate anion), immediately, was added methyl 2-iodo benzoate (0.233 g, 0.89 mmol) in THF (1 M solution) in one shot. After 30 min, completion of the reaction was confirmed by TLC analysis. The reaction mixture was then treated with saturated aqueous NH_4Cl (10 ml), the organic layer was separated. The aqueous layer was extracted with EtOAc (20 mL x 2), the combined organic layers were washed with water, brine, dried over $NaSO_4$, filtered and the solvents were removed under reduced pressure. The crude product was purified by column chromatography (silica gel, 50% EtOAc/ Pet ether) to obtain the desired isocoumarin **12** (0.294 g, 81%) as white solid.



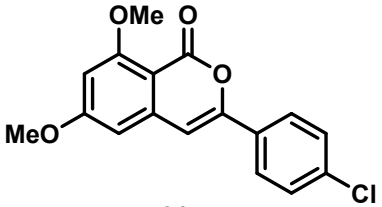
19

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96-7.94 (d, *J* = 8 Hz, 1H), 7.43-7.40 (t, *J* = 15, 7.5 Hz, 1H), 7.12-7.09 (t, *J* = 15.5, 7.5 Hz, 1H), 6.55 (s, 1H), 6.50-6.49 (d, *J* = 2Hz, 1H), 6.44-6.43 (d, *J* = 2.5 Hz, 1H), 4.00 (s, 3H), 3.92 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) 165.5, 163.4, 156.3, 141.6, 140.1, 137.9, 131.0, 130.4, 128.1, 125.4, 107.0, 103.4, 100.6, 99.1, 96.3, 56.3, 55.7. IR (neat, cm^{-1}) 2966, 1737, 1607, 1577, 1370, 1223, 1131, 995. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{17}H_{13}IO_4$ 408.9931; Found 408.9921. Melting point 161-163 °C.



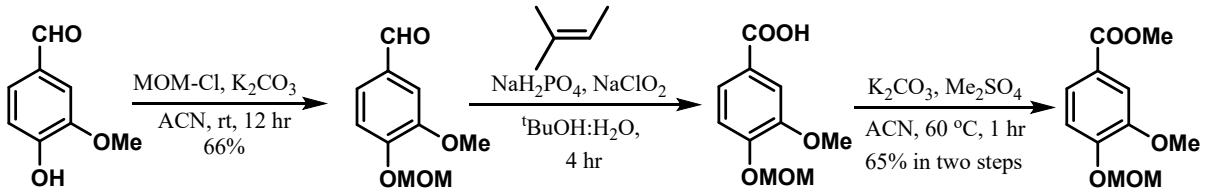
20

3-(3-chlorophenyl)-6,8-dimethoxy-1H-isochromen-1-one, (20): Conditions B was followed for the synthesis of the isocoumarin **20**. The product **20** was obtained as white solid (0.126 g, 84%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.76-7.72 (m, 1H), 7.37-7.36 (m, 2H), 6.74 (s, 1H), 6.43-6.42 (q, *J* = 4, 2 Hz, 2H), 3.97 (s, 3H), 3.91(s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) 165.4, 163.4, 157.9, 152.9, 141.8, 135.1, 133.8, 130.0, 129.9, 125.4, 123.4, 103.6, 102.6, 100.6, 99.1, 56.2, 55.6. IR (neat, cm^{-1}) 2934, 1735, 1606, 1577, 1478, 1372, 1225, 1169. 1063. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{17}H_{13}ClO_4$ 317.0575; Found 317.0571. Melting point 164-166 °C.



21

3-(4-chlorophenyl)-6,8-dimethoxy-1H-isochromen-1-one, (21): Conditions B was followed for the synthesis of the isocoumarin **21**. The product **21** was obtained as pale-yellow liquid (0.125 g, 83%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81-7.80 (d, *J* = 8.5 Hz, 2H), 7.43-7.41 (s, *J* = 8.5 Hz, 2H), 6.77 (s, 1H), 6.48-6.47 (d, *J* = 4 Hz, 2H), 3.99 (s, 3H), 3.92 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) 165.5, 163.4, 158.6, 153.3, 142.0, 136.0, 130.4, 129.0, 126.7, 103.4, 102.2, 100.6, 99.0, 56.4, 55.7. IR (neat, cm^{-1}) 2949, 1736, 1607, 1467, 1373, 1225, 1168. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{17}H_{13}ClO_4$ 317.0575; Found 317.0567.

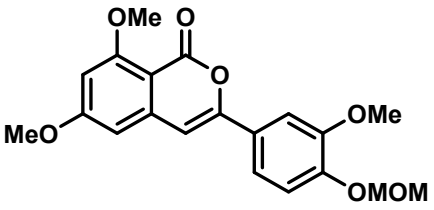


22b 22c 22a

Preparation of methyl 3-methoxy-4-(methoxymethoxy)benzoate, (22a): To a stirred suspension of vanillin (1 g, 6.57 mmol) and K_2CO_3 (1.816g, 13.14 mmol) in acetonitrile (10 mL), MOM chloride (0.75 mL, 9.9 mmol) was added dropwise. The reaction mixture was stirred overnight at room temperature and the completion was confirmed by TLC analysis. The reaction mixture was washed with water (50 mL), extracted with EtOAc (25 mL x 3). The combined organic layer was dried over anhydrous Na_2SO_4, concentrated under vacuum and purified by column chromatography (silica gel, petroleum ether:EtOAc = 7:1) to obtain the corresponding MOM protected aldehyde **22b** (0.85 g, 66 % yield). The aldehyde was used directly for next step without further purification.

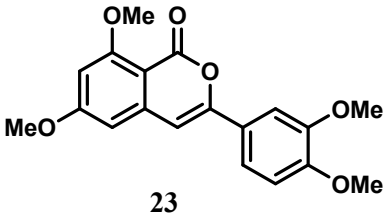
To a stirred solution of aldehyde **22b** (0.85 g, 4.33 mmol) and NaH_2PO_4 (1.82 g, 15.17 mmol) in *t*-BuOH (15 mL) and H_2O (5 mL), $NaClO_2$ (2.349 g, 25.98 mmol) was slowly added in H_2O (5 mL). After stirring at 25 ^oC for 12 h, the reaction mixture was treated with brine (30 mL), the aqueous layer was washed with ether (2 x 30 mL). The combined organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product obtained was directly used for the next step.

To a stirred suspension of crude acid **22c** (0.8 g) and K_2CO_3 (6 g, 45 mmol) in acetonitrile (30 mL), was added Me_2SO_4 (4.2 mL, 45 mmol). The reaction mixture was heated at 60 ^oC for 1 hr. The completion of the reaction was confirmed by TLC analysis. After cooling, the reaction mixture was washed with water (20 mL), extracted with EtOAc (25 mL x 3). The combined organic layer was dried over anhydrous Na_2SO_4, concentrated under vacuum and purified by column chromatography (silica gel, petroleum ether:EtOAc = 7:1) to obtain the corresponding ester **22a** (2.1 g, 65% in overall two steps) as pale-yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.62-7.60 (dd, *J* = 8.5, 2 Hz, 1H), 7.55 (s, 1H), 7.16-7.14 (d, *J* = 8.5 Hz, 1H), 5.28 (s, 2H), 3.94 (s, 3H), 3.90 (s, 3H), 3.51 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 166.5, 152.9, 148.6, 123.5, 122.7, 112.0, 110.2, 94.9, 56.3, 55.8, 51.9. IR (neat, cm^{-1}) 2987, 1721, 1606, 1520, 1442, 1277, 1224, 1141, 912, 736. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{11}H_{14}O_5$ 226.0841; Found 226.0842.



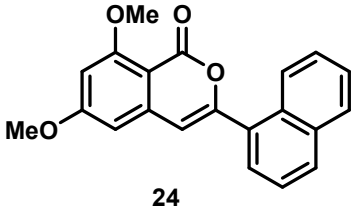
22

6,8-dimethoxy-3-(3-methoxy-4-(methoxymethoxy)phenyl)-1H-isochromen-1-one, (19): Conditions A was followed for the synthesis of the isocoumarin **22**. The product **22** was obtained as pale-yellow liquid (0.147 g, 83%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41-7.39 (d, *J* = 6.5 Hz, 2H), 7.21-7.19 (d, *J* = 9 Hz, 1H), 6.71 (s, 1H), 6.46 (s, 1H), 5.28 (s, 2H), 3.98 (s, 6H), 3.92 (s, 3H), 3.53 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) 165.5, 163.4, 159.0, 154.3, 149.8, 148.2, 142.5, 126.3, 118.5, 115.9, 108.9, 103.2, 101.1, 100.2, 98.6, 95.3, 56.4, 56.3, 55.7. IR (neat, cm^{-1}) 2936, 1736, 1608, 1525, 1474, 1254, 1171, 1002. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{20}H_{20}O_7$ 373.1282; Found 373.1284.



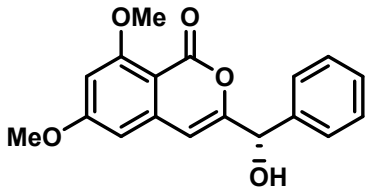
23

3-(3,4-dimethoxyphenyl)-6,8-dimethoxy-1H-isochromen-1-one, (23): Conditions A was followed for the synthesis of the isocoumarin **23**. The product **23** was obtained as pale-yellow liquid (0.15 g, 92%).^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47-7.46 (d, *J* = 5 Hz, 1H), 7.36 (s, 1H), 6.93-6.91 (d, *J* = 8.15 Hz, 1H), 6.69 (s, 1H), 6.45 (s, 1H), 3.98 (s, 6H), 3.94 (s, 3H), 3.92 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) 165.4, 163.4, 159.0, 154.4, 150.7, 149.2, 142.6, 124.8, 118.7, 111.1, 100.8, 100.2, 98.5, 56.4, 56.2, 56.0, 55.7. IR (neat, cm^{-1}) 2952, 1733, 1605, 1524, 1473, 1262, 1004. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{19}H_{18}O_6$ 343.1172; Found 343.1176.



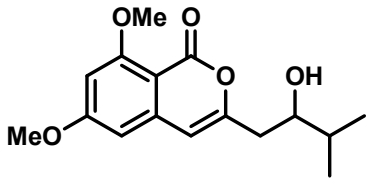
24

6,8-dimethoxy-3-(naphthalen-1-yl)-1H-isochromen-1-one, (24): Conditions A was followed for the synthesis of the isocoumarin **24**. The product **24** was obtained as white solid (0.143 g, 91%).^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24-8.22 (d, *J* = 8 Hz, 1H), 7.90-7.85 (m, 2H), 7.72-7.71 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.53-7.47 (m, 3H), 6.59 (s, 1H), 6.48-6.47 (d, *J* = 2 Hz, 1H), 6.43-6.42 (d, *J* = 2.5 Hz, 1H), 3.99 (s, 3H), 3.90 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) 165.4, 163.4, 158.8, 155.6, 142.1, 133.8, 130.8, 130.7, 130.4, 128.5, 127.5, 127.0, 126.2, 125.3, 125.0, 107.1, 103.4, 100.3, 98.9, 56.2, 55.6. IR (neat, cm^{-1}) 2952, 1732, 1605, 1464, 1371, 1223, 1135, 995. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{21}H_{16}O_4$ 333.1115; Found 333.1121. Melting point 148-150 °C.



25

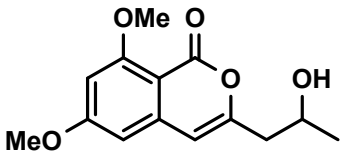
(S)-3-(hydroxy(phenyl)methyl)-6,8-dimethoxy-1H-isochromen-1-one, (25): Conditions A was followed for the synthesis of the isocoumarin **25**. The product **25** was obtained as pale-yellow liquid (0.093 g, 63%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47-7.46 (d, *J* = 7.5 Hz, 2H), 7.40-7.34 (m, 3H), 6.45 (s, 1H), 6.36 (s, 1H), 6.32 (s, 1H), 5.52 (s, 1H), 3.95 (s, 3H), 3.87 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) 165.5, 163.4, 158.2, 141.6, 139.2, 128.7, 128.6, 127.0, 103.0, 100.6, 100.0, 99.0, 72.9, 56.3, 55.7. IR (neat, cm^{-1}) 3367, 2941, 1721, 1607, 1465, 1216, 1167, 1067. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{18}H_{16}O_5$ 313.1071; Found 313.1068. $[\alpha]_{25}^{D}$ = +2.5 (0.2 M in CH_2Cl_2).



26

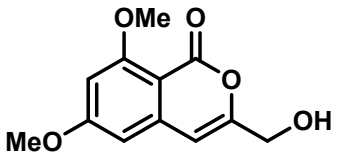
3-(2-hydroxy-3-methylbutyl)-6,8-dimethoxy-1H-isochromen-1-one, (26): Conditions A was followed for the synthesis of the isocoumarin **26**. The product **26** was obtained as pale-yellow liquid (48%).^{1}H NMR (500 MHz, $CDCl_3$) δ 6.29-6.28 (d, *J* = 2 Hz, 1H), 6.194-6.190 (d, *J* = 2 Hz, 1H), 6.09 (s, 1H), 3.87 (s, 3H), 3.80 (s, 3H), 2.60-2.57 (dd, *J* = 14.5, 2.5 Hz, 1H), 2.40-2.35 (dd, *J* = 14.5, 9.5 Hz, 1H), 1.73-1.60 (m, 1H), 0.93-0.91 (dd, *J* = 7, 2.5

Hz, 6H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) 165.3, 163.3, 159.0, 156.6, 142.1, 105.0, 103.1, 99.5, 98.2, 73.3, 56.1, 55.4, 38.7, 33.7, 18.8, 17.3. IR (neat, cm^{-1}) 3386, 2978, 1727, 1608, 1470, 1218, 912. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{16}H_{20}O_5$ 265.1071; Found 265.1069.



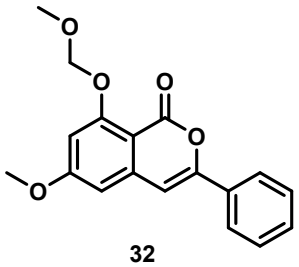
27

3-(2-hydroxypropyl)-6,8-dimethoxy-1H-isochromen-1-one, (27):[10] Conditions A was followed for the synthesis of the isocoumarin **27**. The product **27** was obtained as yellow liquid (0.054 g, 43%).^1H NMR (500 MHz, $CDCl_3$) δ 6.44 (s, 3H), 6.33 (s, 3H), 6.20 (s, 3H), 4.32-4.24 (m, 2H), 3.96 (s, 3H), 3.89 (s, 3H), 2.65-2.53 (m, 2H), 2.10-2.01 (m, 2H), 1.29-1.28 (d, J = 5 Hz, 6H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) 165.2, 163.1, 159.3, 156.0, 142.1, 105.1, 102.8, 99.5, 98.1, 65.1, 55.9, 55.4, 43.2, 23.1. IR (neat, cm^{-1}) 3352, 2945, 1734, 1610, 1469, 1381, 1249, 1172. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{14}H_{16}O_5$ 265.1071; Found 265.1069.



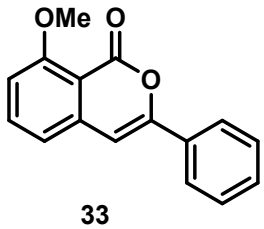
28

3-(hydroxymethyl)-6,8-dimethoxy-1H-isochromen-1-one, (28): Conditions A was followed for the synthesis of the isocoumarin **28**. The product **28** was obtained as pale-yellow liquid (0.050 g, 45%). ^1H NMR (500 MHz, $CDCl_3$) δ 6.48-6.47 (d, J = 2.5 Hz, 1H), 6.393-6.388 (d, J = 2.5 Hz, 1H), 6.380 (s, 1H), 4.43 (s, 2H), 3.97 (s, 3H), 3.90 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) 165.6, 163.4, 156.4, 141.7, 103.3, 102.9, 100.4, 98.8, 61.4, 56.3, 55.7. IR (neat, cm^{-1}) 3388, 2940, 1740, 1602, 1265, 1111. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{18}H_{16}O_5$ 267.0863; Found 267.0860.



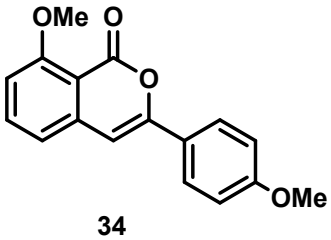
32

6-methoxy-8-(methoxymethoxy)-3-phenyl-1H-isochromen-1-one, (32): Conditions A was followed for the synthesis of the isocoumarin **32**. The product **32**was obtained as pale-yellow liquid (0.070 g, 54%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88-7.87 (d, *J* = 7 Hz, 2H), 7.47-7.40 (m, 3H), 6.79 (s, 1H), 6.77-6.76 (d, *J* = 2 Hz, 1H), 6.54-6.53 (d, *J* = 2 Hz, 1H), 5.38 (s, 2H), 3.91 (s, 3H), 3.57 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) 167.5, 165.1, 161.1, 154.3, 141.9, 130.9, 130.0, 128.9, 128.8, 125.4, 104.3, 102.6, 102.3, 101.8, 95.1, 56.6, 55.6; IR (neat, cm^{-1}) 2945, 1740, 1609, 1372, 1167. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{18}H_{16}O_5$ 313.1071; Found 313.1065.



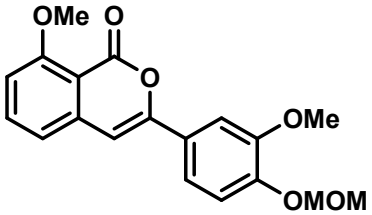
33

8-methoxy-3-phenyl-1H-isochromen-1-one, (33):[7] Conditions A was followed for the synthesis of the isocoumarin **33**. The product **33** was obtained as yellow liquid (0.107 g, 89%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82-7.80 (d, *J* = 7.5 Hz, 2H), 7.57-7.54 (t, *J* = 16, 8 Hz, 1H), 7.40-7.35 (m, 3H), 7.04-7.03 (d, *J* = 8 Hz, 1H), 6.95-6.94(d, *J* = 8 Hz, 1H), 6.86 (s, 1H), 4.02 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) 161.7, 159.1, 154.0, 140.5, 135.8, 131.9, 130.0, 128.8, 125.3, 118.1, 109.9, 109.3, 101.8, 56.4. IR (neat, cm^{-1}) 2938, 1743, 1652, 1606, 1576, 1484, 1284, 1116. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{16}H_{12}O_3$ 253.0859; Found 253.0857.



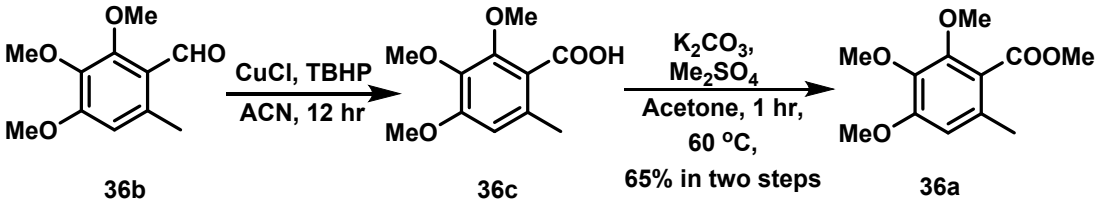
34

8-methoxy-3-(4-methoxyphenyl)-1H-isochromen-1-one, (34):[11] Conditions A was followed for the synthesis of the isocoumarin **34**. The product **34** was obtained as yellow liquid (0.114 g, 85%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82-7.80 (d, *J* = 9 Hz, 2H), 7.60-7.57 (t, *J* = 16,8 Hz, 1H), 7.00-6.88 (m, 4H), 6.72 (s, 1H), 4.01 (s, 3H), 3.85 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) 161.7, 161.1, 159.2, 154.0, 140.9, 135.7, 126.9, 124.4, 117.9, 114.2, 109.4, 108.9, 100.2, 56.3, 55.4. IR (neat, cm^{-1}) 2951, 1726, 1610, 1467, 1219, 1169, 1061. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{17}H_{14}O_4$ 283.0964; Found 283.0968.



35

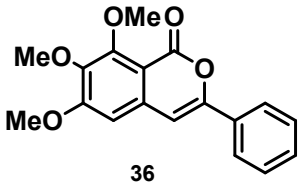
8-methoxy-3-(3-methoxy-4-(methoxymethoxy)phenyl)-1H-isochromen-1-one, (35): Conditions A was followed for the synthesis of the isocoumarin **35**. The product **35** was obtained as yellow solid (0.130 g, 80%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61-7.57 (t, *J* = 16, 8 Hz, 1H), 7.41 (s, 1H), 7.19-7.18 (d, *J* = 9Hz, 1H), 7.01-6.99 (d, *J* = 7.5 Hz, 1H), 6.92-6.90 (d, *J* = 8.5 Hz, 1H), 6.74 (s, 1H), 5.27 (s, 2H), 4.03 (s, 3H), 3.99 (s, 3H), 3.53 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) 161.7, 159.2, 153.8, 149.8, 148.1, 140.7, 135.8, 126.2, 122.9, 122.6, 118.4, 117.9, 115.9, 109.6, 108.8, 100.9, 95.3, 56.32, 56.28, 56.21. IR (neat, cm^{-1}) 2951, 1726, 1610, 1467, 1219, 1169, 1061. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{19}H_{18}O_6$ 343.1176; Found 343.1172.



36b 36c 36a

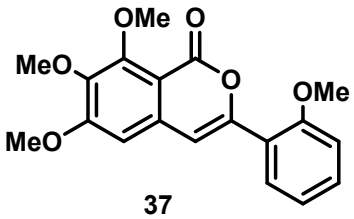
Preparation of methyl 2,3,4-trimethoxy-6-methylbenzoate, (36a): A similar procedure to that used for the preparation of **6** was followed to obtain the ester **36a** (2.1 g, 65% in overall two steps) as yellow oil, starting from aldehyde **36b**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.45 (s, 1H), 3.87(s, 6H), 3.84(s, 3H), 3.81(s, 3H), 2.25(s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 168.0, 154.3, 151.3, 140.0, 131.5, 121.4, 109.2, 61.6, 60.8, 55.9, 51.9, 19.6. IR

(neat, cm^{-1}) 2977, 1730, 1610, 1472, 1355, 1265, 1211, 1150. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{12}H_{16}O_5$ 241.1071; Found 241.1072.



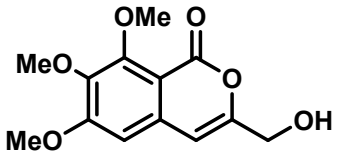
36

6,7,8-trimethoxy-3-phenyl-1H-isochromen-1-one, (36):[12] Conditions A was followed for the synthesis of the isocoumarin **36**. The product **36** was obtained as yellow liquid (0.136 g, 93%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.85-7.84 (d, *J* = 7.5 Hz, 2H), 7.45-7.40 (m, 3H), 6.81 (s, 1H), 6.69 (s, 1H), 4.01 (s, 3H), 3.98 (s, 3H), 3.92 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) 159.1, 158.6, 155.7, 153.3, 142.8, 136.2, 131.8, 129.8, 128.7, 125.1, 108.0, 103.3, 101.5, 61.9, 61.4, 56.2. IR (neat, cm^{-1}) 2952, 1734, 1600, 1498, 1345, 1261, 1117, 1002. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{18}H_{16}O_5$ 313.1071; Found 313.1068.



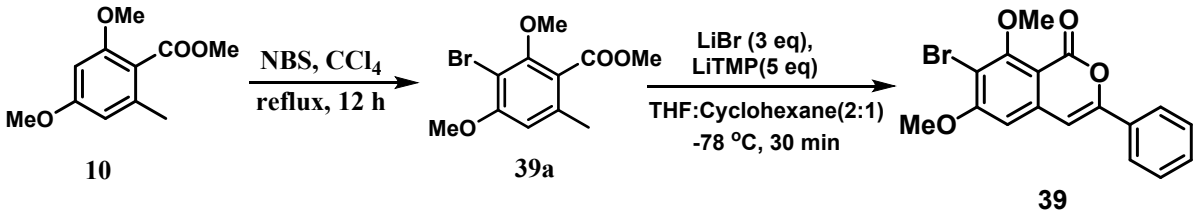
37

6,7,8-trimethoxy-3-(2-methoxyphenyl)-1H-isochromen-1-one, (37): Conditions A was followed for the synthesis of the isocoumarin **37**. The product **37** was obtained as yellow liquid (0.143 g, 88%). ^1H NMR (500 MHz, $CDCl_3$) δ 8.00-7.98 (dd, *J* = 7.5,1.5 Hz, 1H), 7.38-7.34 (t, *J* = 14, 7 Hz, 1H), 7.24 (s, 1H), 7.08-7.05 (t, *J* = 15, 7.5 Hz, 1H), 7.00-6.98 (d, *J* = 8.5 Hz, 1H), 6.67 (s, 1H), 4.02 (s, 3H), 3.99 (s, 3H), 3.97 (s, 3H), 3.93 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) 158.9, 158.6, 157.2, 155.7, 150.2, 142.8, 136.8, 130.6, 128.9, 121.0, 120.7, 111.3, 108.4, 106.7, 103.6, 61.9, 61.4, 56.1, 55.6. IR (neat, cm^{-1}) 2946, 1732, 1598, 1499, 1375, 1261, 1116, 912. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{19}H_{18}O_6$ 343.1176; Found 343.1172.



38

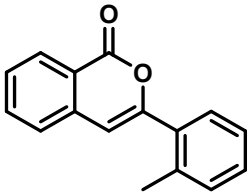
3-(hydroxymethyl)-6,7,8-trimethoxy-1H-isochromen-1-one, (38): Conditions A was followed for the synthesis of the isocoumarin **38**. The product **38** was obtained as yellow liquid (0.062 g, 49%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (s, 1H), 6.36 (s, 1H), 4.43 (s, 2H), 3.98 (s, 3H), 3.96 (s, 3H), 3.90 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) 167.4, 159.3, 158.3, 156.0, 155.7, 143.0, 135.7, 108.2, 103.1, 102.4, 61.9, 61.3, 56.1. IR (neat, cm^{-1}) 3296, 2945, 1736, 1655, 1452, 1404, 1293, 1117. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{13}H_{14}O_6$ 267.0863; Found 267.0860.



10 39a 39

Preparation of methyl-3-bromo-2,4-dimethoxy-6-methylbenzoate, (39a):[2] To a stirred solution of ester **10**[1] (0.11 g, 0.52 mmol) in CCl_4 (2 mL), was added NBS (0.103 g, 0.58 mmol). The reaction mixture was refluxed for 12 hr. The completion of the reaction was confirmed by TLC. The reaction mixture was washed with H_2O (20 mL), extracted with EtOAc (30 mL x 3). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, concentrated under vacuum and purified by column chromatography (silica gel, petroleum ether:EtOAc = 7:1) to obtain the corresponding ester **39a** (0.086 g, 57%) as yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$+ CCl_4) δ 6.35 (s, 1H), 3.89 (s ,3H), 3.88 (s, 3H), 3.82 (s, 3H), 2.32 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$+CCl_4) δ 168.1, 157.3, 156.5, 137.0, 117.7, 105.7, 93.9, 56.3, 56.1, 52.3, 20.5. IR (neat cm^{-1}) 2968, 1733, 1604, 1443, 1285, 1118, 1021. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{11}H_{13}BrO_4$ 289.0070, 291.0050; Found 289.0065, 291.0047.

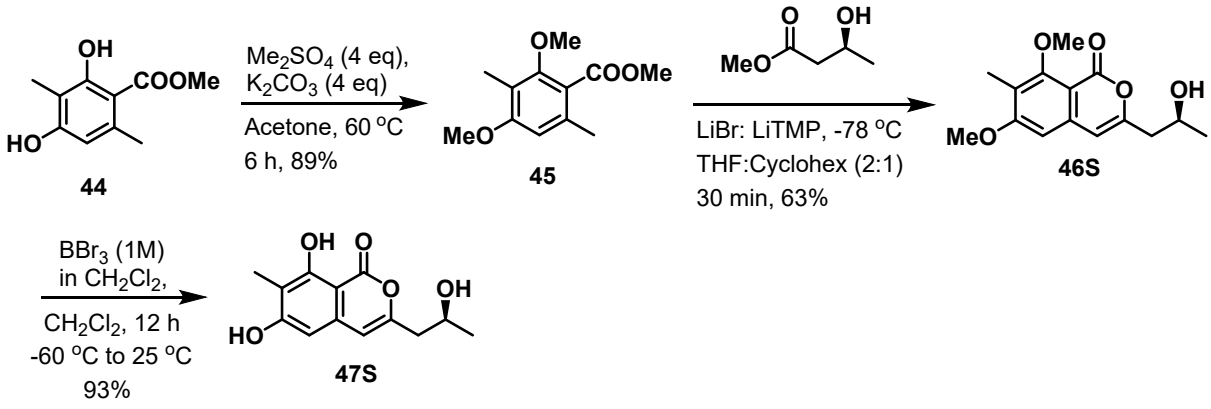
7-bromo-6,8-dimethoxy-3-phenyl-1H-isochromen-1-one, (39): Conditions A was followed for the synthesis of the isocoumarin **39**. The product **39** was obtained as white solid (0.152 g, 89%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93-7.92 (d, *J* = 6.5 Hz, 2H), 7.48-7.43 (m, 3H), 7.31 (s, 1H), 6.50 (s, 1H), 4.04 (s, 3H), 4.01 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) 163.1, 161.4, 158.0, 155.1, 140.0, 131.9, 130.3, 128.8, 125.7, 104.0, 100.6, 99.4, 94.8, 56.4. IR (neat, cm^{-1}) 2964, 1730, 1650, 1591, 1457, 1338, 1227,1011. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{17}H_{13}BrO_4$ 361.0070, 363.0050; Found 361.0067, 363.0045. Melting point 195-197 °C.



40

3-(o-tolyl)-1H-isochromen-1-one, (40):[6] Conditions A was followed for the synthesis of the isocoumarin **40**. The product **40** was obtained as pale-yellow liquid (0.073 g, 65%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39-8.37 (d, *J* = 7.5 Hz, 1H), 7.80-7.77 (t, *J* = 14, 7 Hz, 1H), 7.59-7.52 (m, 3H), 7.41-7.39 (t, *J* = 13, 6.5 Hz, 1H), 7.34-7.32 (d, *J* = 7.5 Hz, 2H), 6.66 (s, 1H), 2.56 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) 162.6, 155.6, 137.5, 136.8, 134.9, 132.8, 131.1, 129.8, 129.7, 129.2, 128.3, 126.0, 125.8, 120.4, 105.9, 20.8. IR (neat, cm^{-1}) 2964, 1728, 1611, 1469, 1284, 1161, 1102. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{16}H_{12}O_2$ 237.0921; Found 237.0916.

Preparation of (*S*)-lunatinin:



Preparation of methyl 2,4-dimethoxy-3,6-dimethylbenzoate, (45):[5] To a stirred suspension of methyl 2,4-dihydroxy-3,6-dimethylbenzoate **44** (2 g, 11 mmol) and K_2CO_3 (6 g, 44 mmol) in acetone (30 mL), was added Me_2SO_4 (4.0 mL, 44 mmol). The reaction mixture was heated at 60 °C for 1 hr. The completion of the reaction was confirmed by TLC analysis. After cooling, the reaction mixture was washed with water (20 mL), extracted with EtOAc (25 mL x 3). The combined organic layer was dried over anhydrous Na_2SO_4, concentrated under vacuum and purified by column chromatography (silica gel, petroleum ether:EtOAc = 7:1) to obtain the corresponding ester **45** (1.85 g, 81% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.42 (s, 1H), 3.89 (s, 3H), 3.82 (s, 3H), 3.74 (s, 3H), 2.29 (s,

3H), 2.09 (s, 3H).$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 168.7, 159.3, 156.8, 134.6, 120.8, 117.2, 107.7, 61.7, 55.5, 51.9, 19.9, 8.8. IR (neat, cm^{-1}) 2964, 1732, 1587, 1464, 1327, 1156, 1011, 913. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{12}H_{16}O_4$ 224.1048; Found 224.1045.

(*S*)-3-(2-hydroxypropyl)-6,8-dimethoxy-7-methyl-1H-isochromen-1-one (46S): Conditions A was followed for the synthesis of the isocoumarin **46S**. The product **46S** was obtained as light-yellow solid (0.072 g, 63%, recrystallized with EtOAc). $[\alpha]_{25}^{D}$ = +27.0; ^1H NMR (500 MHz, $CDCl_3$) δ 6.42 (s, 1H), 6.17 (s, 1H), 4.31-4.25(m, 1H), 3.89 (s, 3H), 3.81 (s, 3H), 2.62-2.50 (m, 2H), 2.15 (s, 3H), 1.29-1.28 (d, *J* = 6 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) 163.6, 160.8, 159.0, 155.1, 139.0, 121.3, 107.0, 105.0, 101.2, 65.3, 61.3, 55.7, 43.3, 23.3, 8.8. IR (neat, cm^{-1}) 3364, 2946, 1727, 1606, 1465, 1245, 1120, 999. HRMS (ESI-quadrupole) m/z: $[M+H]^+$ Calculated for $C_{15}H_{18}O_5$ 279.1227; Found 279.1229.

(*S*)-lunatinin, (47S):[13] To a stirred solution of compound **47S** (0.07 mg, 0.062 mmol) in CH_2Cl_2 (2 mL) was added BBr_3 (1 mL, 1M in CH_2Cl_2) at -60 °C dropwise manner. The reaction mixture was slowly warmed to room temperature and stirred for 12 h. The completion of the reaction was monitored by TLC analysis. The reaction mixture was poured quickly into pre cooled saturated solution (10 mL) of sodium bicarbonate. The compound was extracted with EtOAc (3 x 15 mL) until there is no product in aqueous layer. Combined organic phase is dried with sodium sulphate and the solvents removed in vacuo. The crude product is purified by a short pad of silica gel column chromatography (30% EtOAc/Pet ether) to obtain lunatinin **47S** (0.058 g, 93%) as white solid. Melting point = 167-168 °C; $[\alpha]_{25}^{D}$ = –19.3 (c 0.3 MeOH); ^1H NMR (500 MHz, $CDCl_3$) δ 11.27 (s, 1H), 6.30 (s, 1H), 6.21 (s, 1H), 4.48-4.43 (m, 1H), 3.00-2.90 (m, 2H), 2.17 (s, 3H), 1.81-1.79 (d, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) 166.2, 161.49, 161.46, 152.9, 136.0, 110.8, 106.2, 102.0, 99.9, 45.2, 44.9, 26.2, 7.8. IR (neat, cm^{-1}) 3384, 2944, 1730, 1690, 1446, 1271, 1120. HRMS (APCI) m/z: $[M+H]^+$ Calculated for $C_{13}H_{14}O_5$ 251.0914; Found 251.0912.

XRD Data of (*S*)-3-(2-hydroxypropyl)-6,8-dimethoxy-7-methyl-1H-isochromen-1-one, 45S:

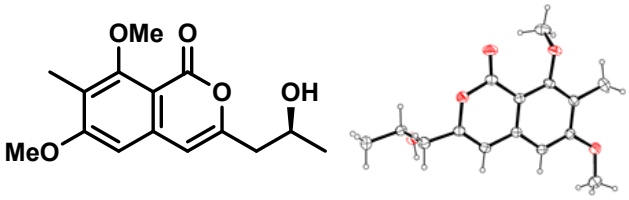


Table 1. Crystal data and structure refinement for (S)-3-(2-hydroxypropyl)-6,8-dimethoxy-7-methyl-1H-isochromen-1-one, 3.

Identification code	shelx	
Empirical formula	C15 H18 O5	
Formula weight	278.29	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 7.4075(3) Å	a= 90°.
	b = 10.2397(5) Å	b= 90°.
	c = 18.5058(9) Å	g = 90°.
Volume	1403.68(11) $Å^3$	
Z	4	
Density (calculated)	1.317 Mg/m^3	
Absorption coefficient	0.099 mm^{-1}	
F(000)	592	
Crystal size	0.095 x 0.078 x 0.068 mm^3	
Theta range for data collection	2.201 to 24.995°.	
Index ranges	-8<=h<=8, -12<=k<=12, -22<=l<=22	
Reflections collected	33358	

Independent reflections	2464 [R(int) = 0.0894]
Completeness to theta = 24.995°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.997 and 0.994
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2464 / 0 / 187
Goodness-of-fit on F^2	1.098
Final R indices [I>2sigma(I)]	R1 = 0.0429, wR2 = 0.0961
R indices (all data)	R1 = 0.0519, wR2 = 0.0978
Absolute structure parameter	0.4(4)
Extinction coefficient	0.047(6)
Largest diff. peak and hole	0.220 and -0.234 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3)
for lunatinin_s. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	7541(3)	5321(3)	5429(1)	47(1)
C(2)	5762(3)	5412(3)	5167(1)	48(1)
C(3)	5257(3)	4619(3)	4599(2)	47(1)
C(4)	6500(3)	3767(3)	4257(1)	43(1)
C(5)	8281(3)	3733(2)	4521(1)	41(1)
C(6)	8779(3)	4501(3)	5111(1)	45(1)
C(7)	9580(3)	2914(3)	4152(1)	47(1)
C(8)	9113(3)	2208(3)	3585(1)	46(1)
C(9)	6007(3)	2954(3)	3642(2)	51(1)
C(10)	10285(4)	1385(3)	3126(2)	54(1)
C(11)	10688(3)	1967(3)	2389(1)	51(1)
C(12)	11863(4)	1072(3)	1951(2)	70(1)
C(13)	9588(4)	5954(4)	6366(2)	78(1)
C(14)	4436(4)	6340(3)	5516(2)	73(1)
C(15)	3018(4)	5461(3)	3807(2)	74(1)
O(1)	7893(2)	6085(2)	6009(1)	62(1)
O(2)	3468(2)	4617(2)	4395(1)	61(1)
O(3)	4549(2)	2841(2)	3363(1)	76(1)
O(4)	7351(2)	2220(2)	3338(1)	56(1)
O(5)	11462(2)	3240(2)	2445(1)	62(1)

XRD Data of (*R*)-3-(2-hydroxypropyl)-6,8-dimethoxy-7-methyl-1H-isochromen-1-one, 43R:

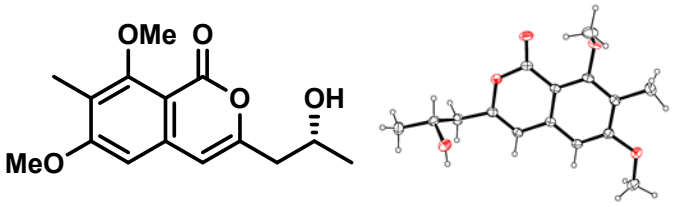


Table 1. Crystal data and structure refinement for (R)-3-(2-hydroxypropyl)-6,8-dimethoxy-7-methyl-1H-isochromen-1-one, 4.

Identification code	shelx	
Empirical formula	C15 H18 O5	
Formula weight	278.29	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 7.3959(5) Å	a= 90°.
	b = 10.1952(7) Å	b= 90°.
	c = 18.4363(13) Å	g = 90°.
Volume	1390.15(17) $Å^3$	
Z	4	
Density (calculated)	1.330 Mg/m^3	
Absorption coefficient	0.100 mm^{-1}	
F(000)	592	
Crystal size	0.095 x 0.085 x 0.075 mm^3	
Theta range for data collection	2.283 to 25.000°.	
Index ranges	-8<=h<=8, -12<=k<=12, -20<=l<=21	
Reflections collected	15831	
Independent reflections	2441 [R(int) = 0.0365]	
Completeness to theta = 25.000°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.993 and 0.991	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2441 / 0 / 182	
Goodness-of-fit on F^2	1.057	
Final R indices [I>2sigma(I)]	R1 = 0.0373, wR2 = 0.0991	

R indices (all data)	R1 = 0.0472, wR2 = 0.1061
Absolute structure parameter	0.2(5)
Extinction coefficient	n/a
Largest diff. peak and hole	0.229 and -0.136 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3)
for lunatinin. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	4244(4)	5416(3)	5167(2)	41(1)
C(2)	4749(4)	4617(3)	4601(2)	39(1)
C(3)	3500(4)	3764(3)	4261(2)	35(1)
C(4)	1720(4)	3726(3)	4520(1)	34(1)
C(5)	1218(4)	4502(3)	5107(2)	39(1)
C(6)	2461(4)	5323(3)	5424(2)	41(1)
C(7)	4001(4)	2950(3)	3645(2)	42(1)
C(8)	889(4)	2198(3)	3585(2)	40(1)
C(9)	423(4)	2909(3)	4156(2)	38(1)
C(10)	412(5)	5966(4)	6362(2)	66(1)
C(11)	5562(5)	6335(4)	5518(2)	62(1)
C(12)	6980(5)	5460(4)	3814(2)	65(1)
C(13)	-285(4)	1378(3)	3123(2)	45(1)
C(14)	-681(4)	1965(3)	2383(2)	43(1)
C(15)	-1868(5)	1061(3)	1946(2)	59(1)
O(1)	2107(3)	6094(2)	6012(1)	53(1)
O(2)	6536(3)	4610(2)	4399(1)	51(1)
O(3)	5460(3)	2834(3)	3366(1)	68(1)
O(4)	2655(3)	2205(2)	3338(1)	47(1)
O(5)	-1458(3)	3236(2)	2444(1)	54(1)

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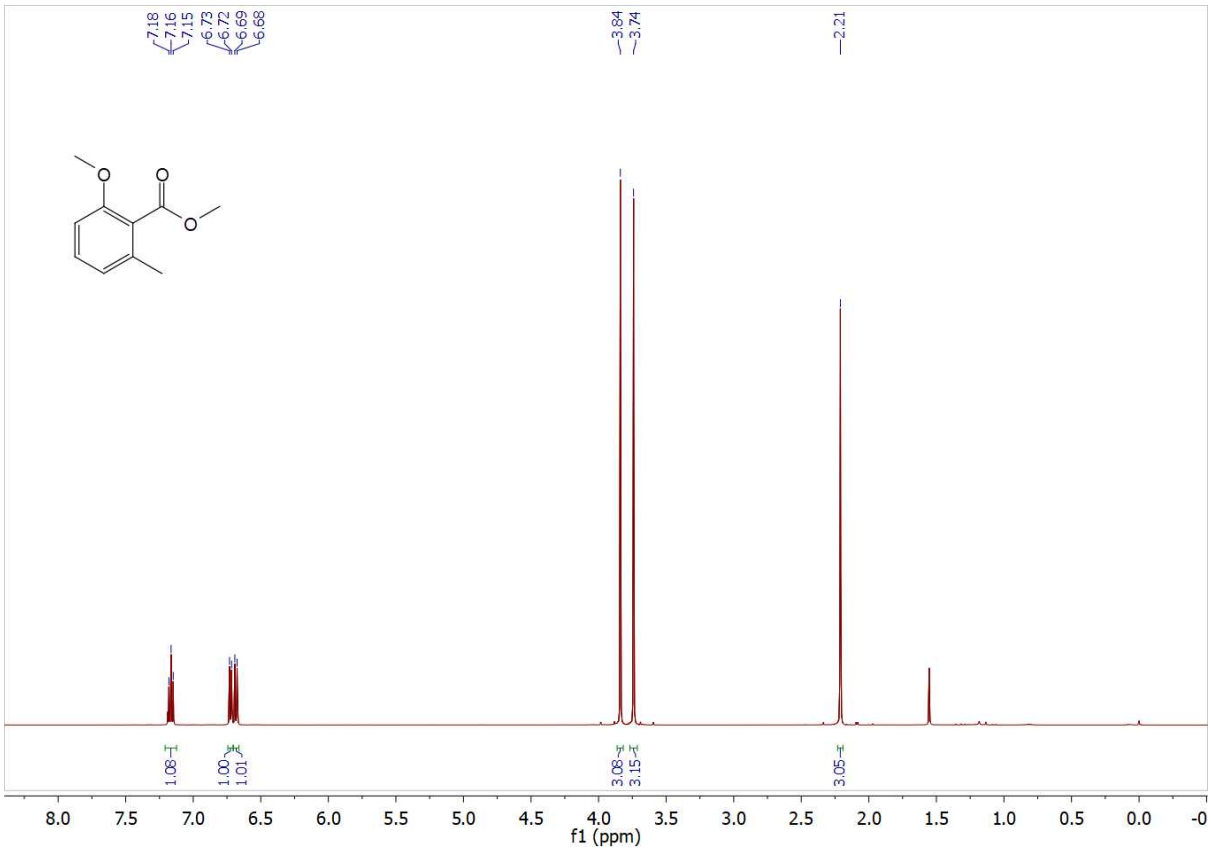
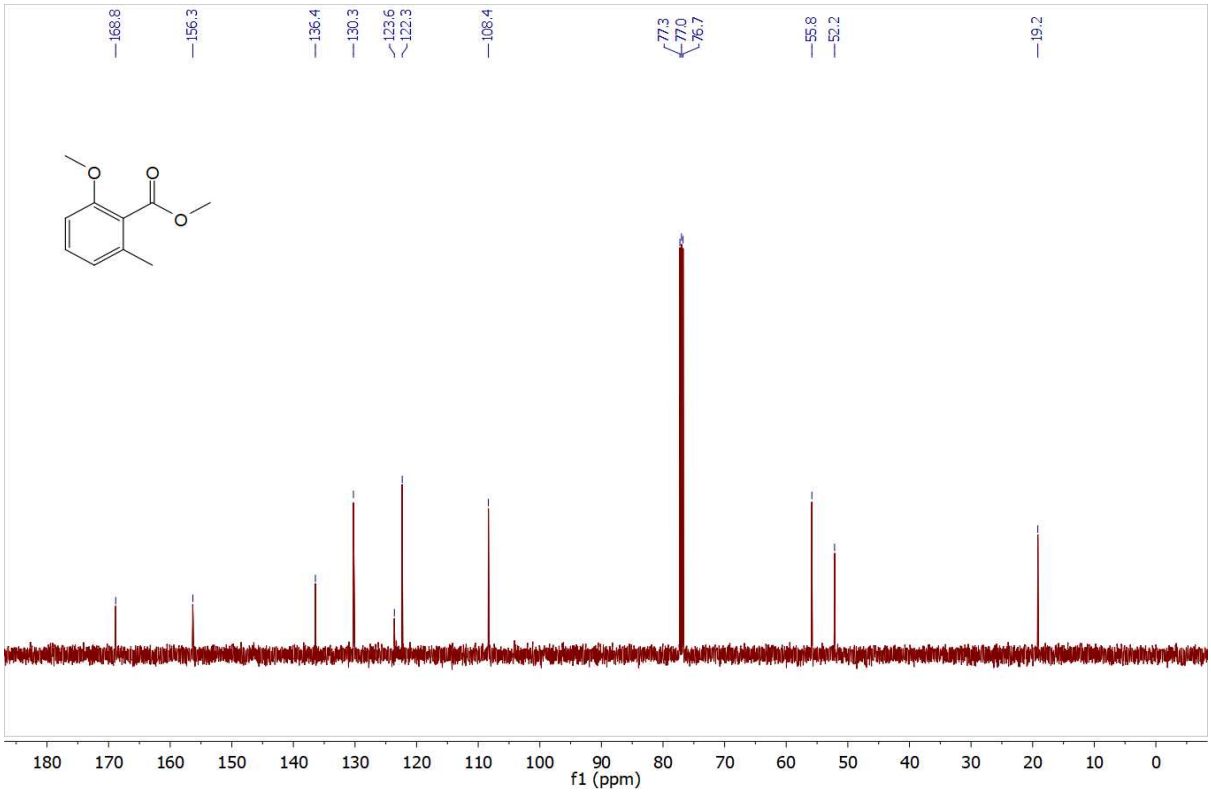
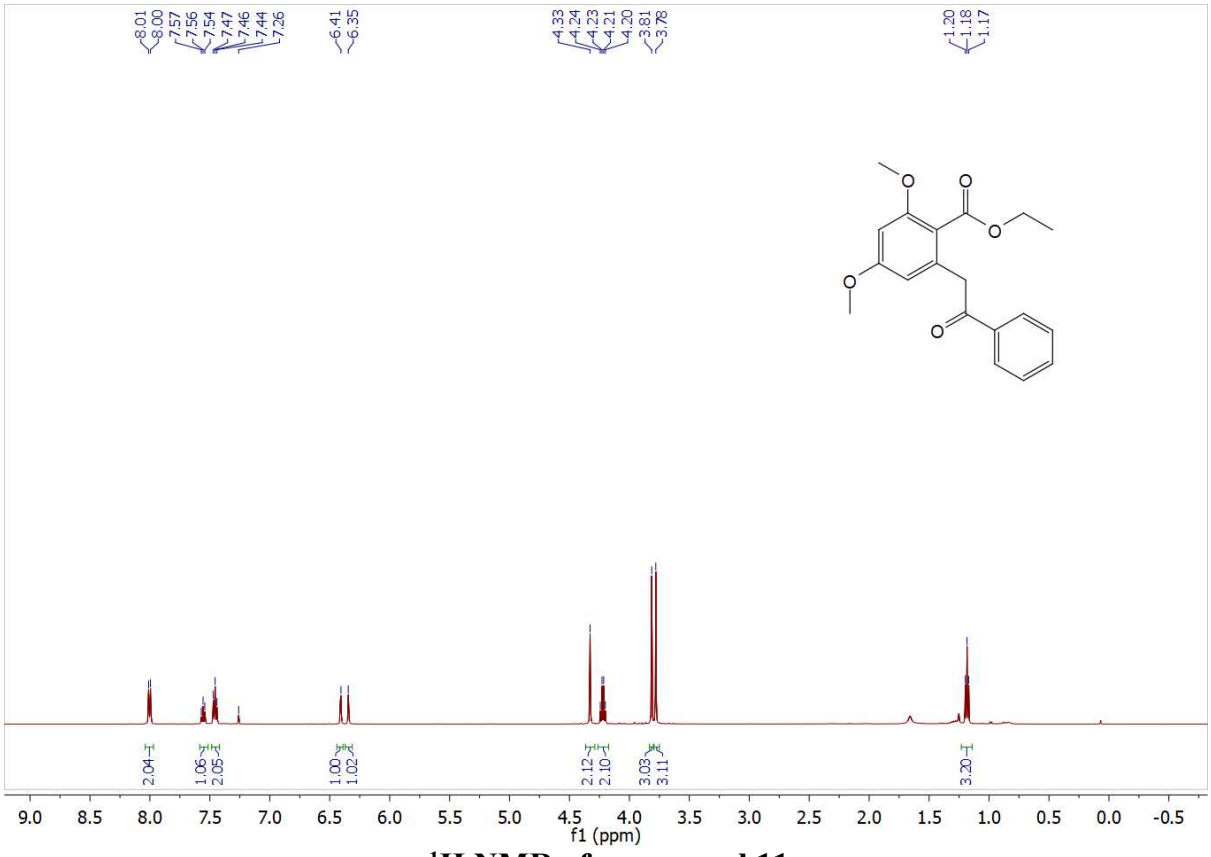
Spectral Data:



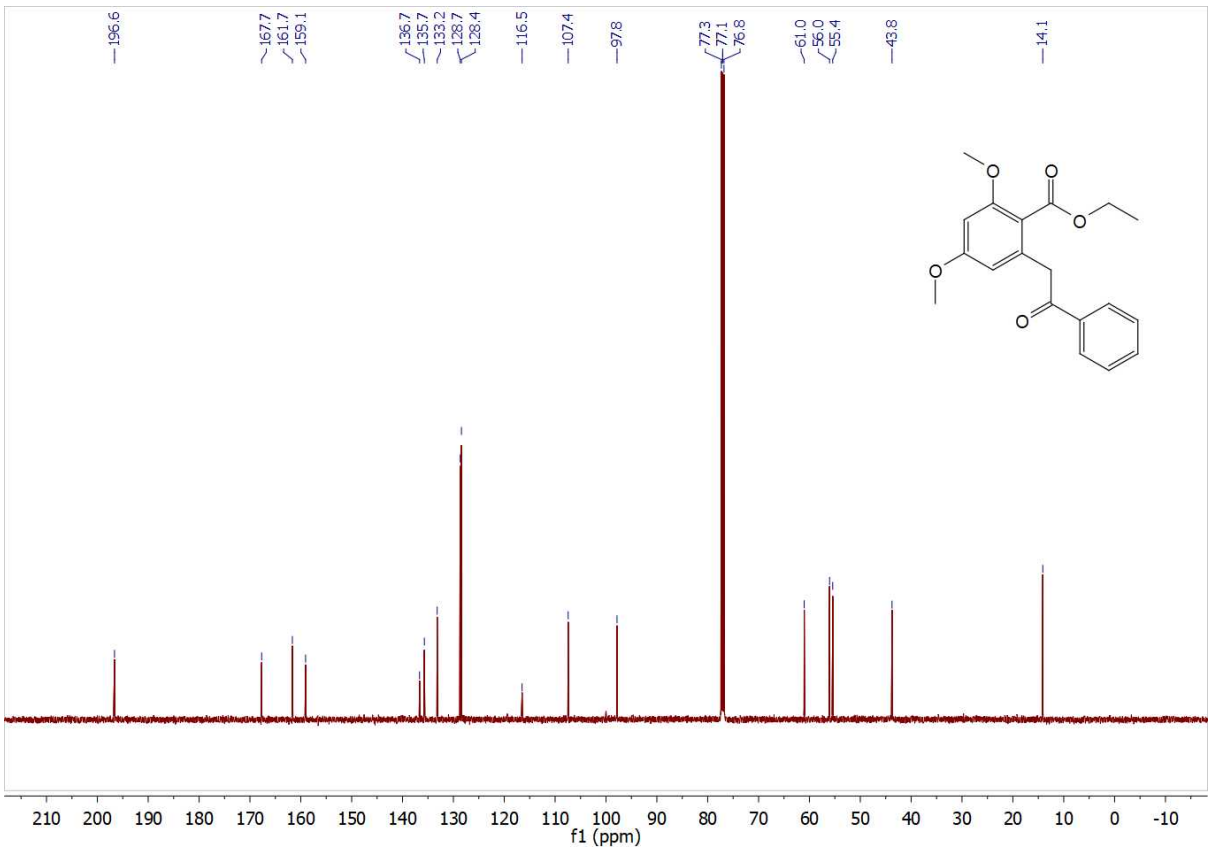
^{1}H NMR of compound 6



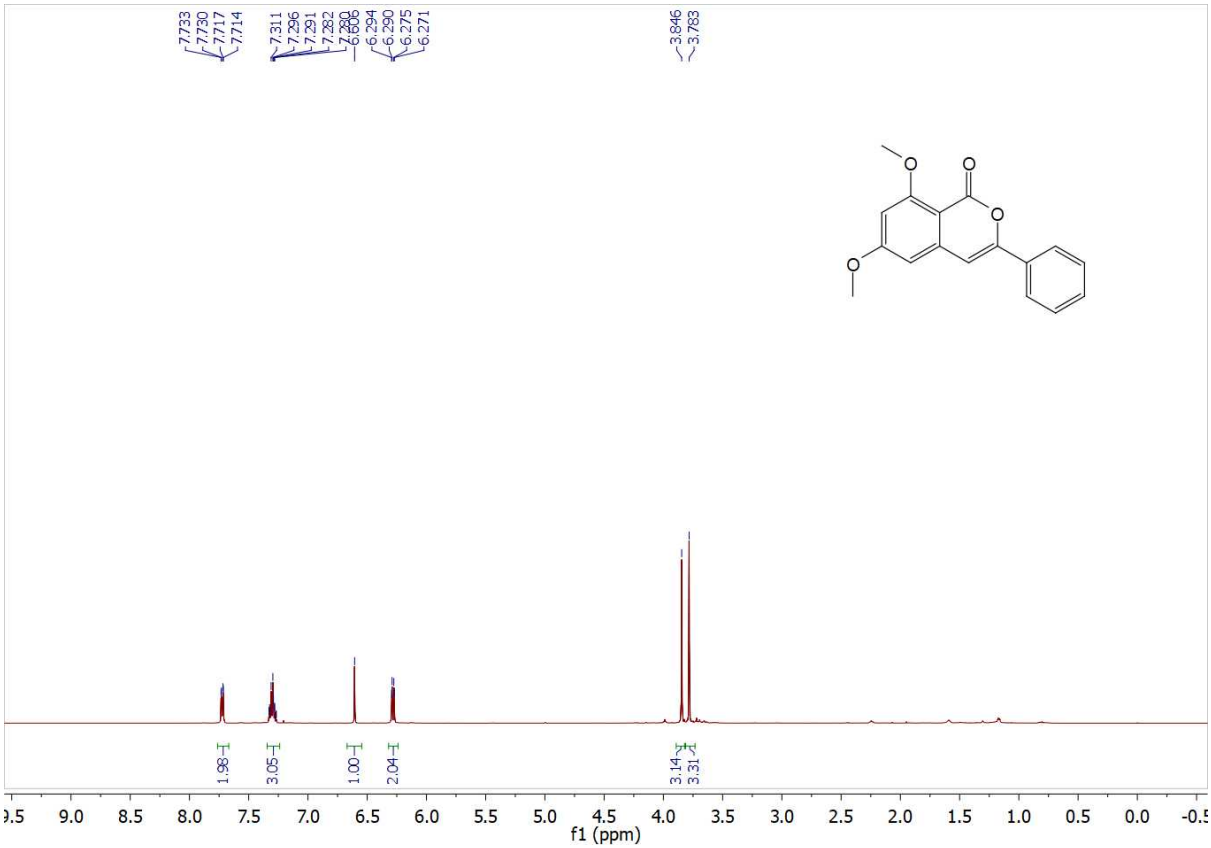
^{13}C{H} NMR of compound 6



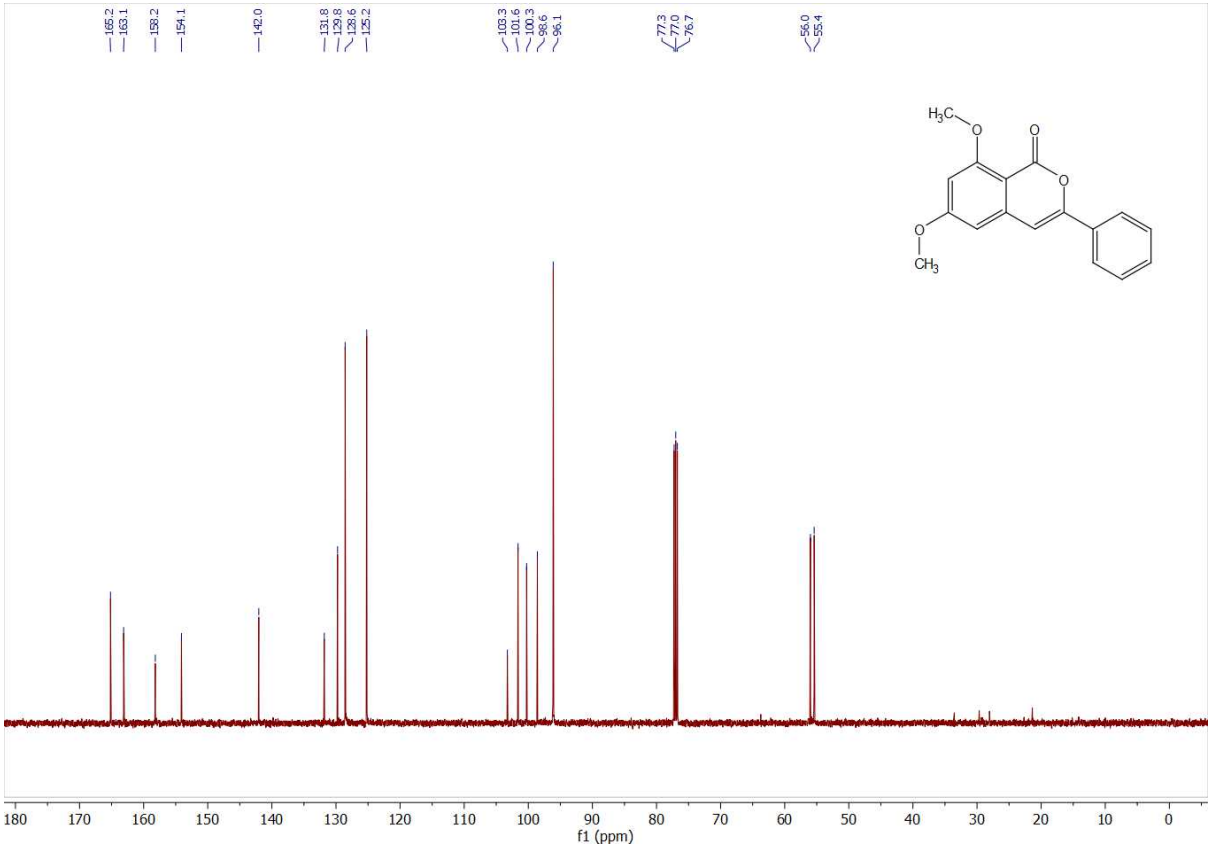
^{1}H NMR of compound 11



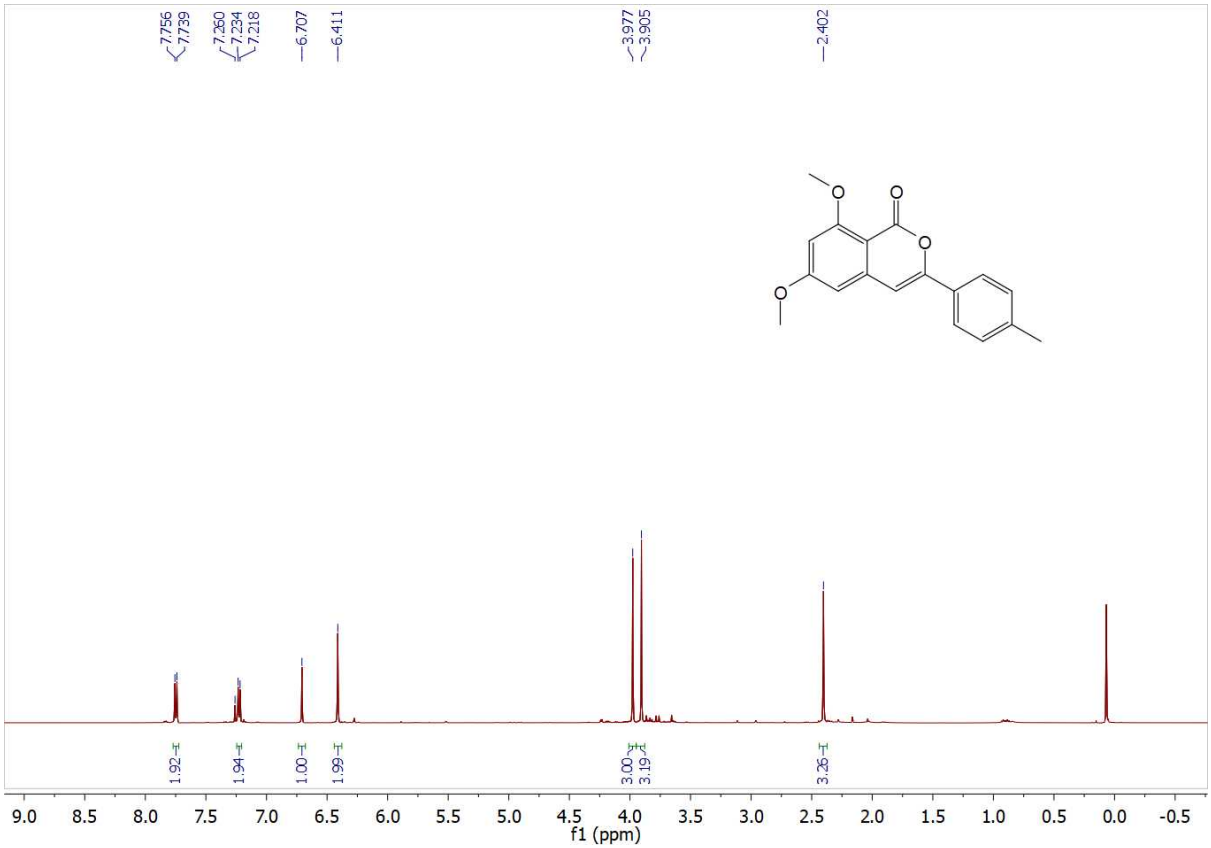
$^{13}C\{H\}$ NMR of compound 11



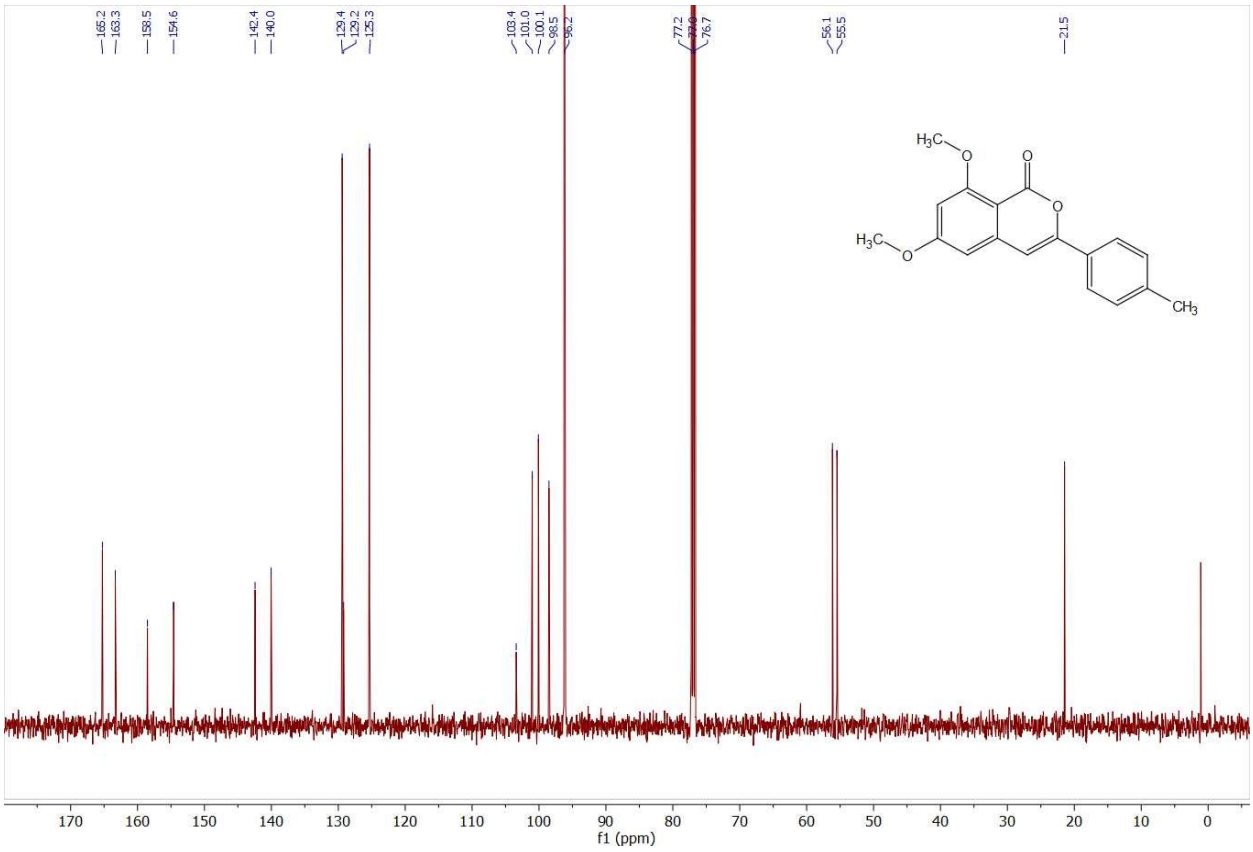
^{1}H NMR of compound 12



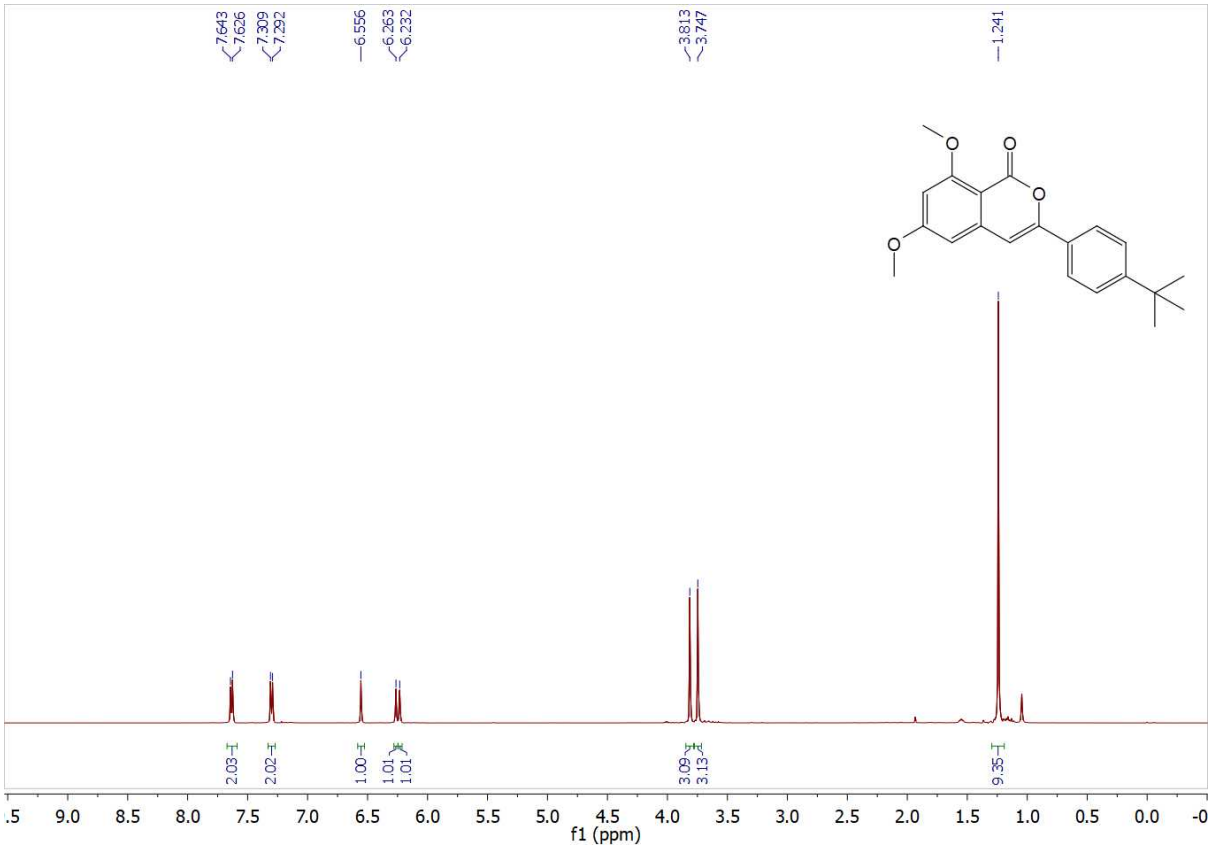
^{13}C{H} NMR of compound 12



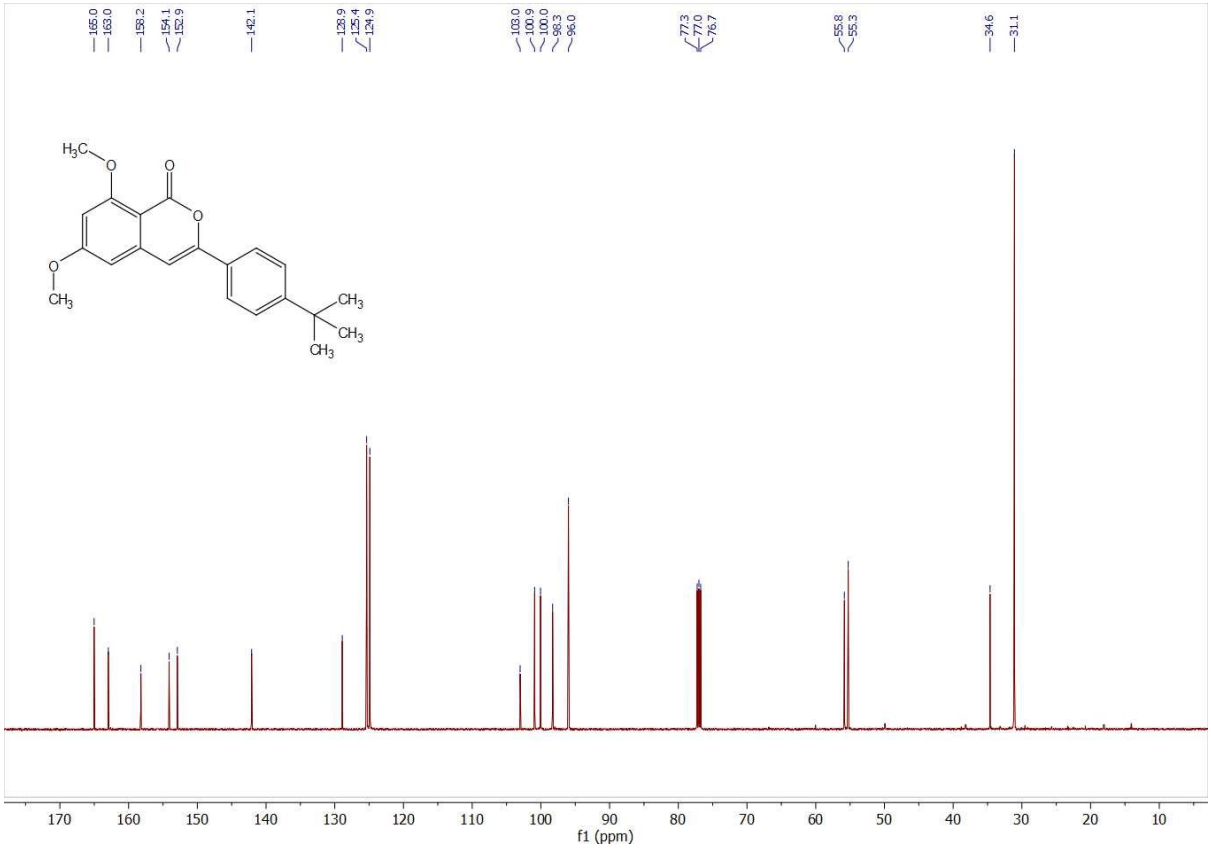
^{1}H NMR of compound 14



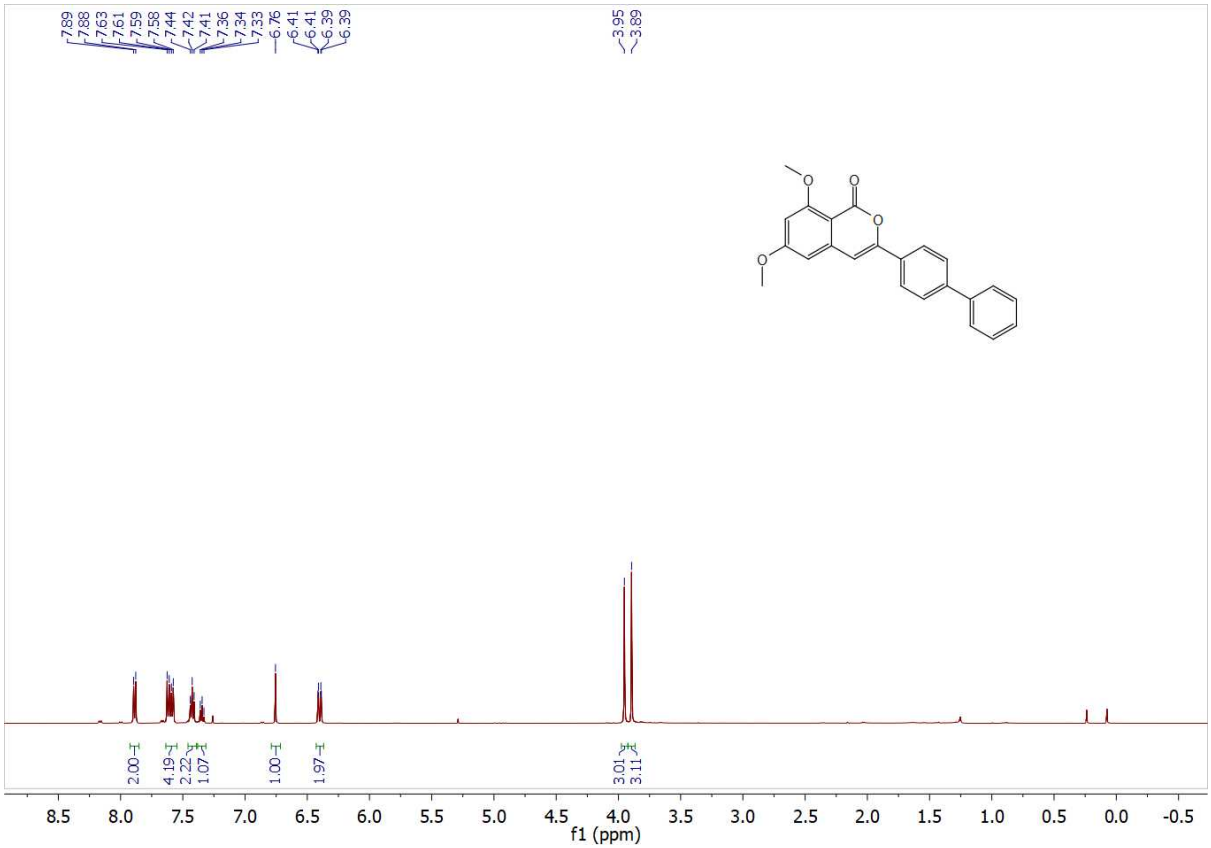
^{13}C{H} NMR of compound 14



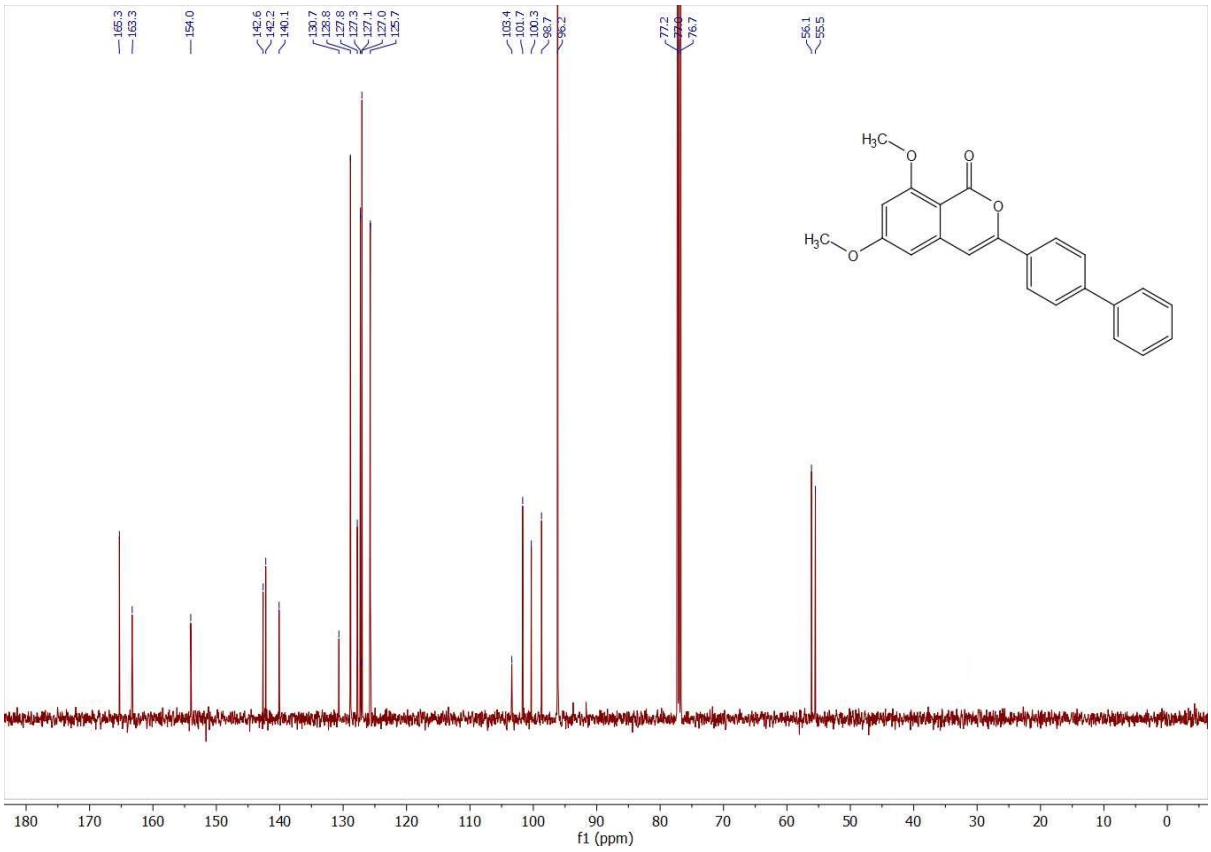
^{1}H NMR of compound 15



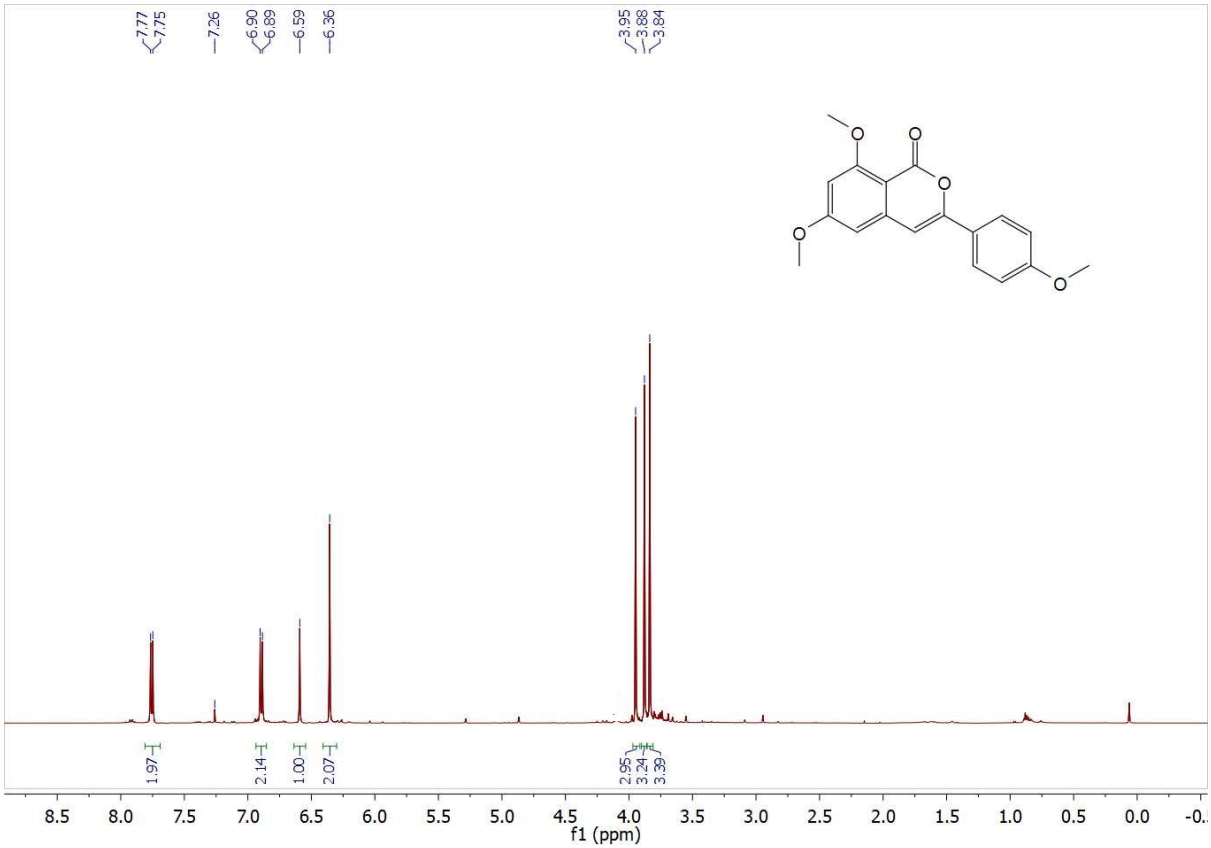
^{13}C{H} NMR of compound 15



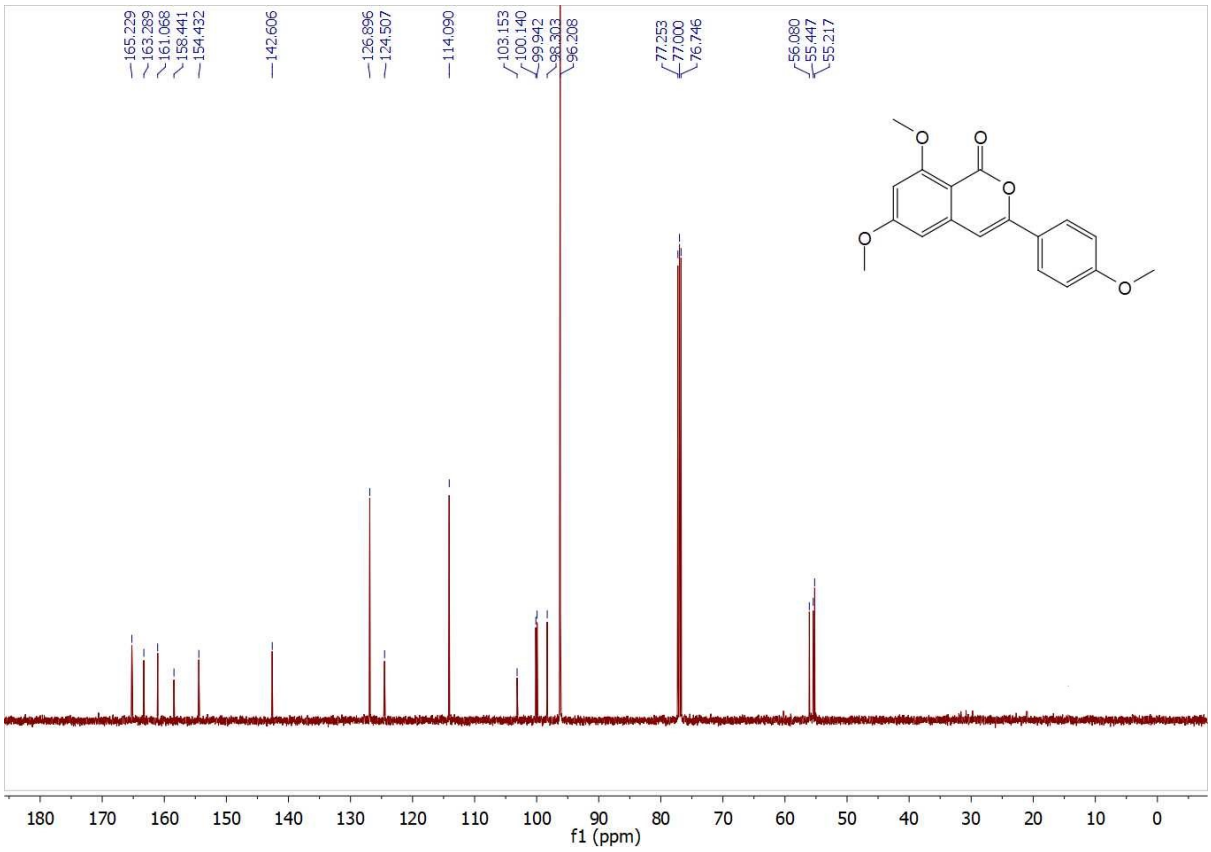
^{1}H NMR of compound 16



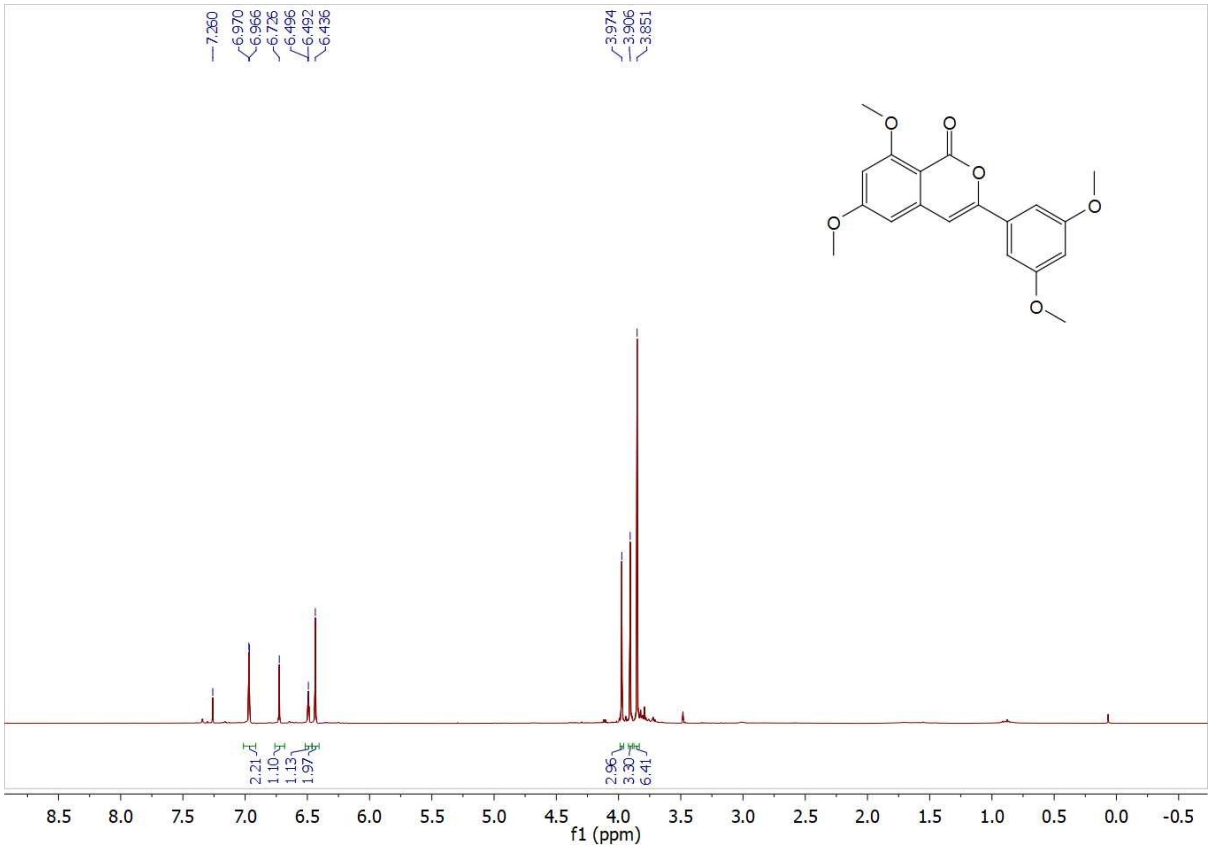
^{13}C{H} NMR of compound 16



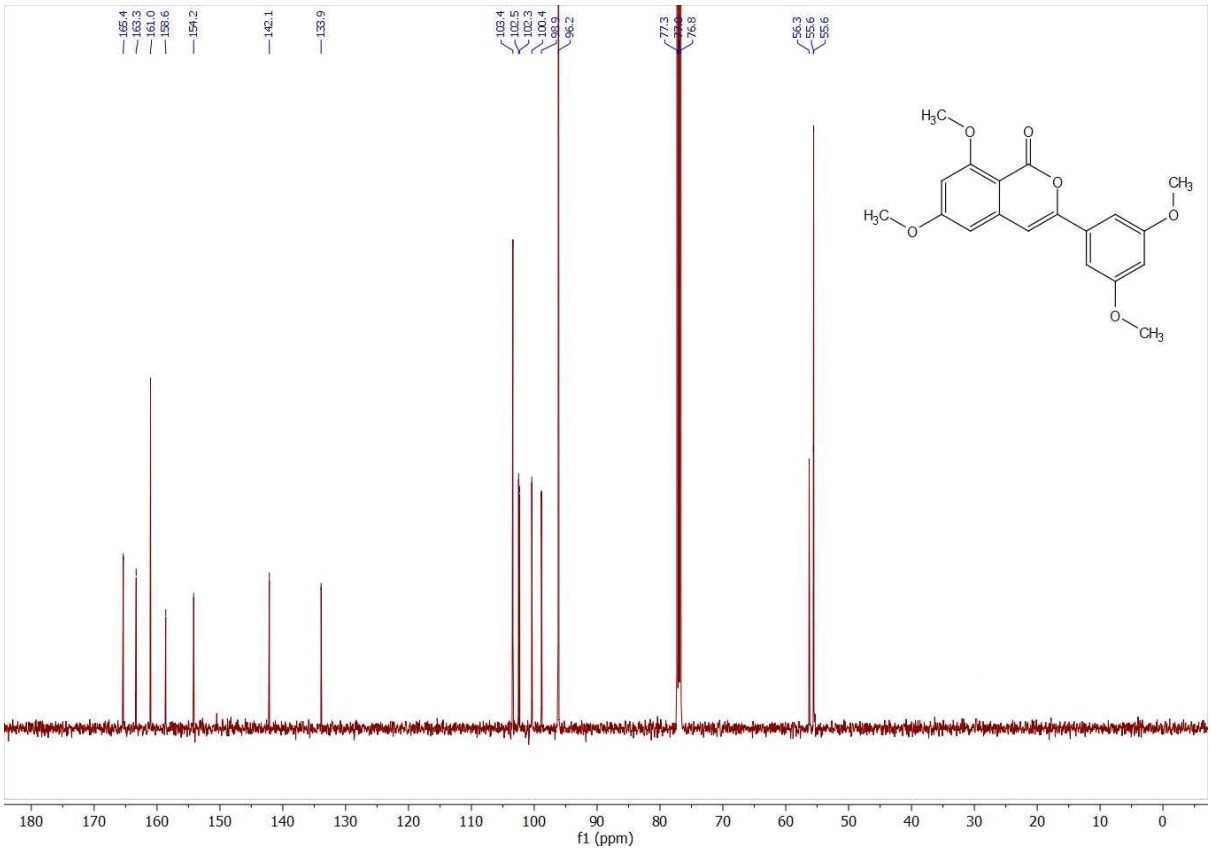
^{1}H NMR of compound 17



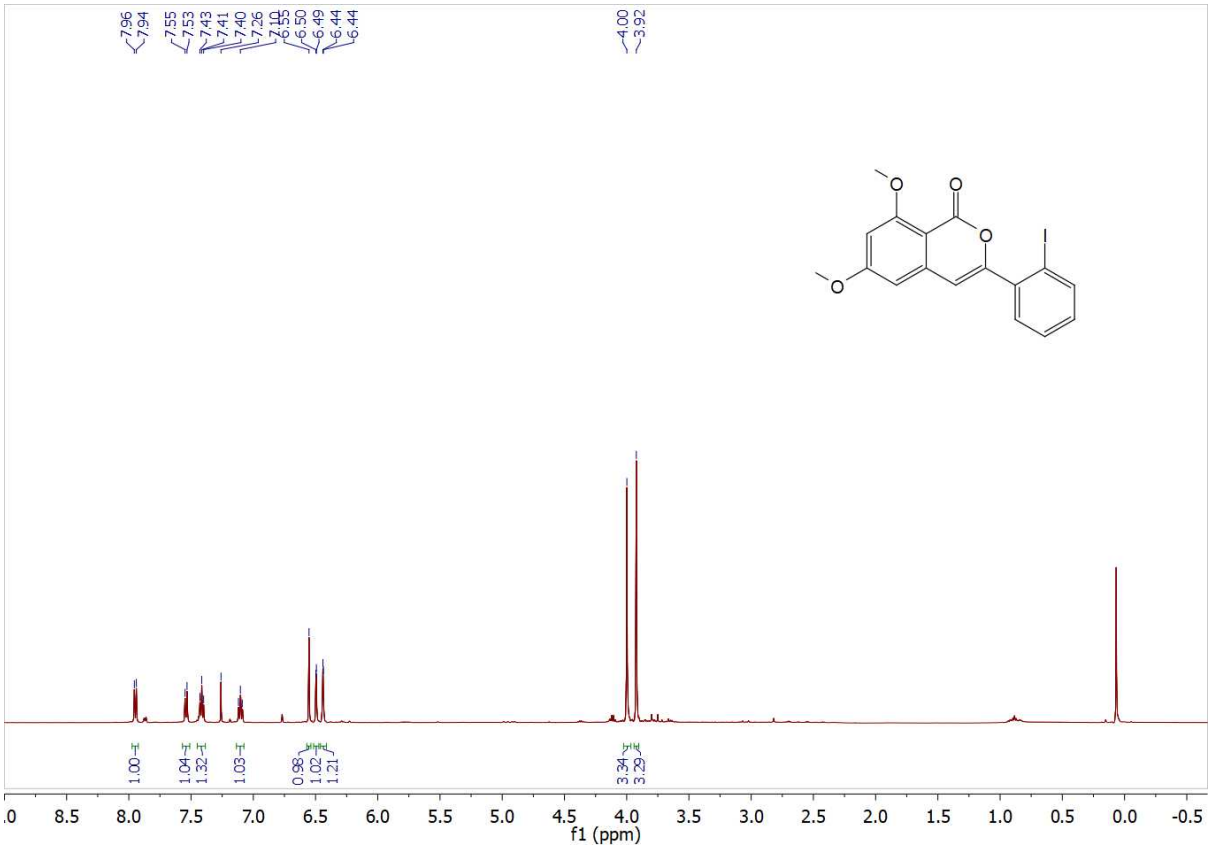
^{13}C{H} NMR of compound 17



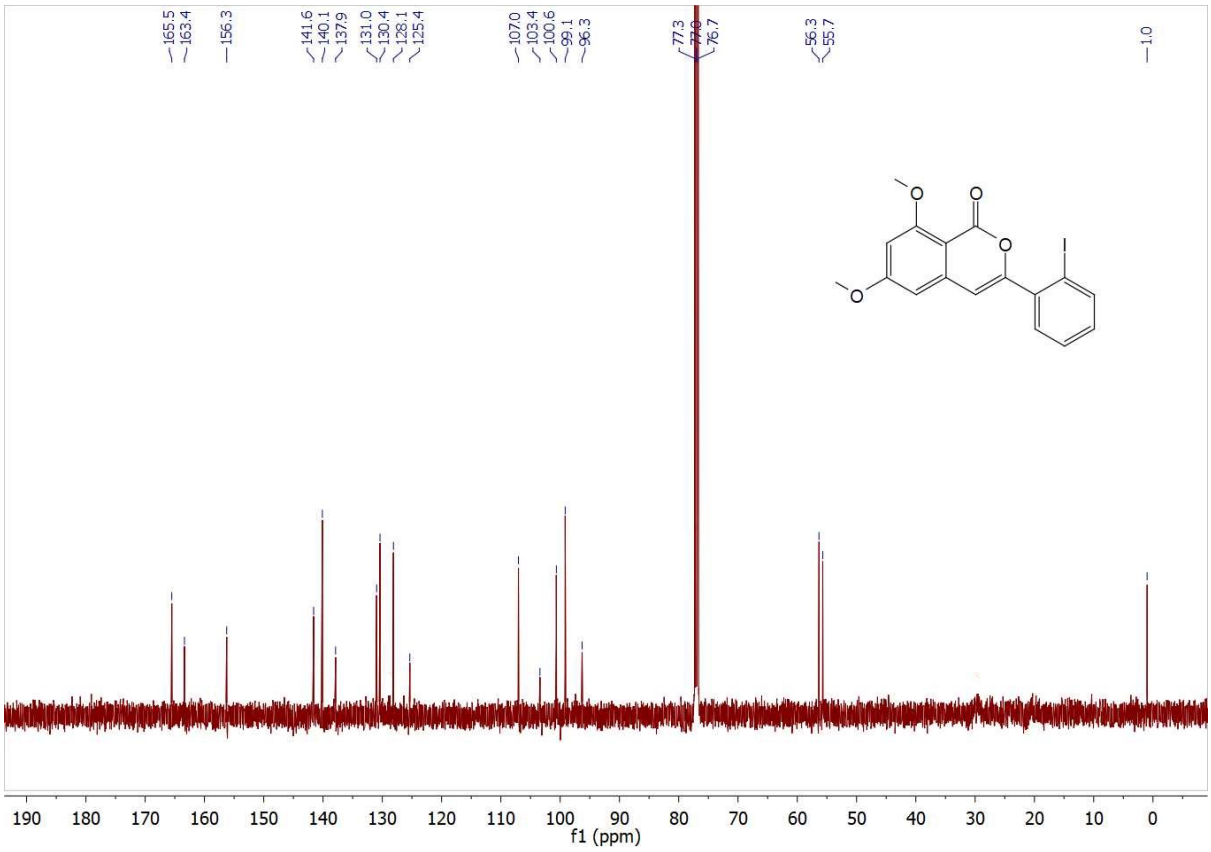
^{1}H NMR of compound 18



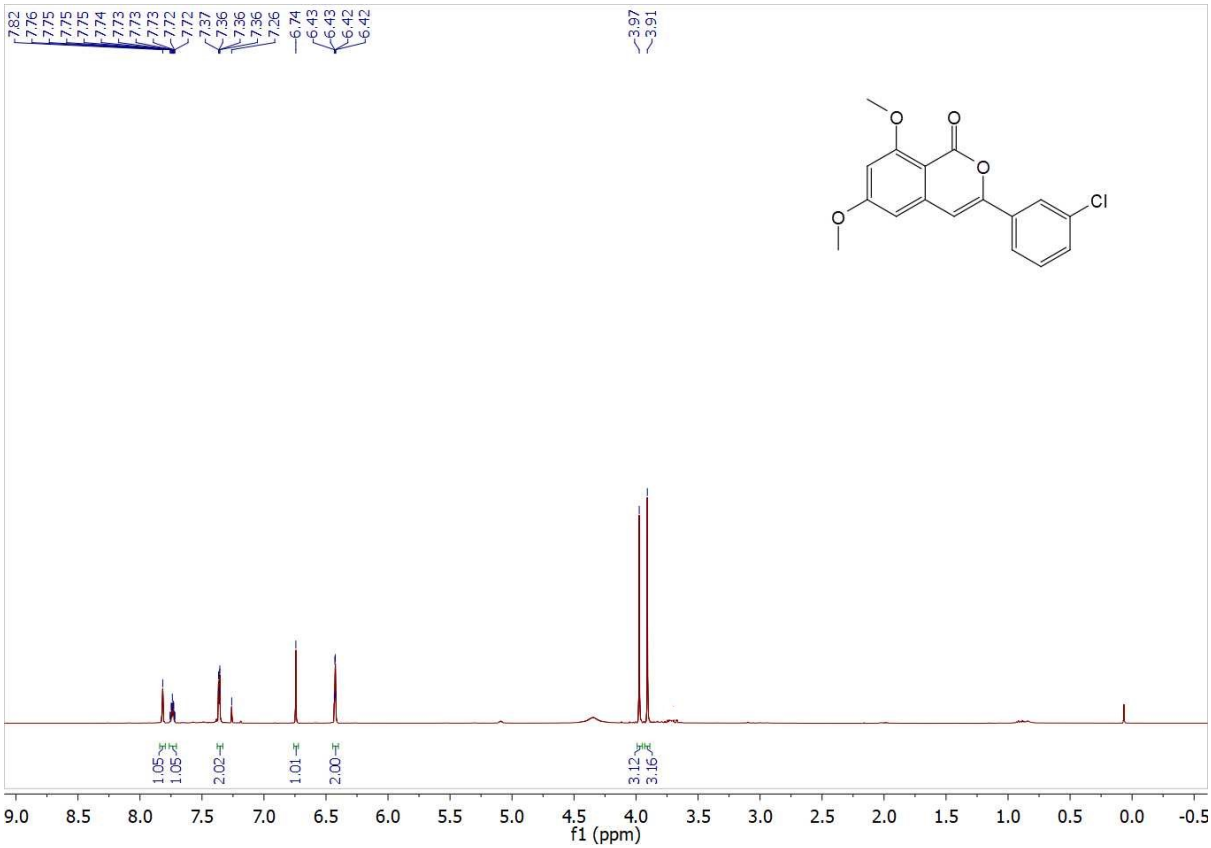
^{13}C{H} NMR of compound 18



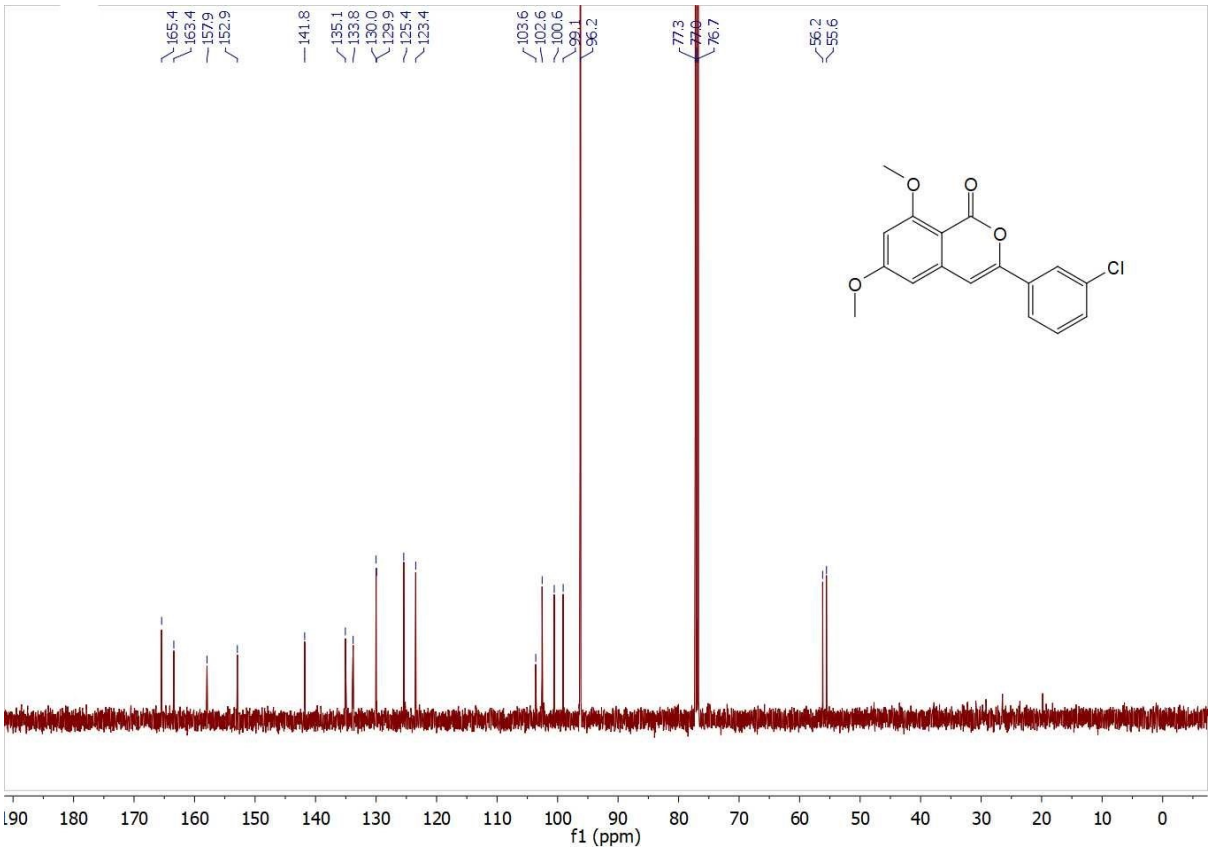
^{1}H NMR of compound 19



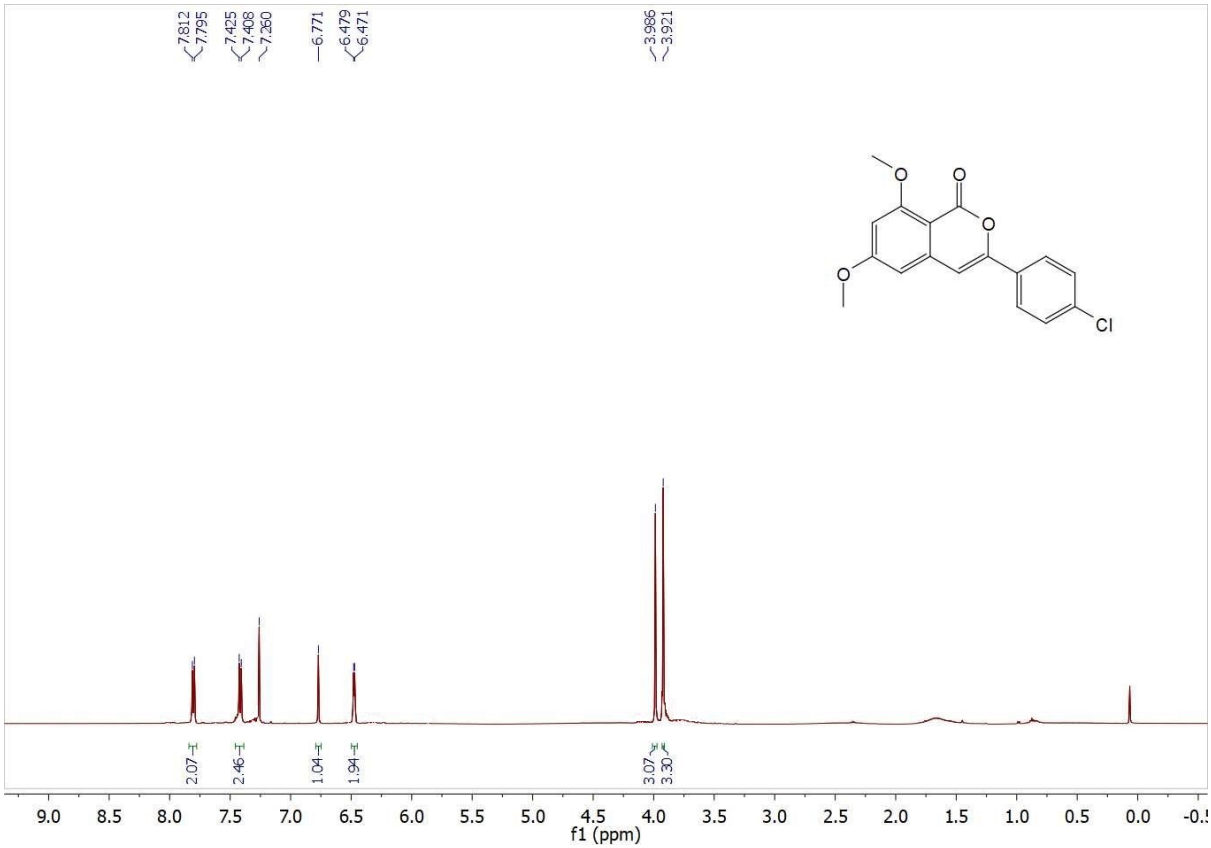
^{13}C{H} NMR of compound 19



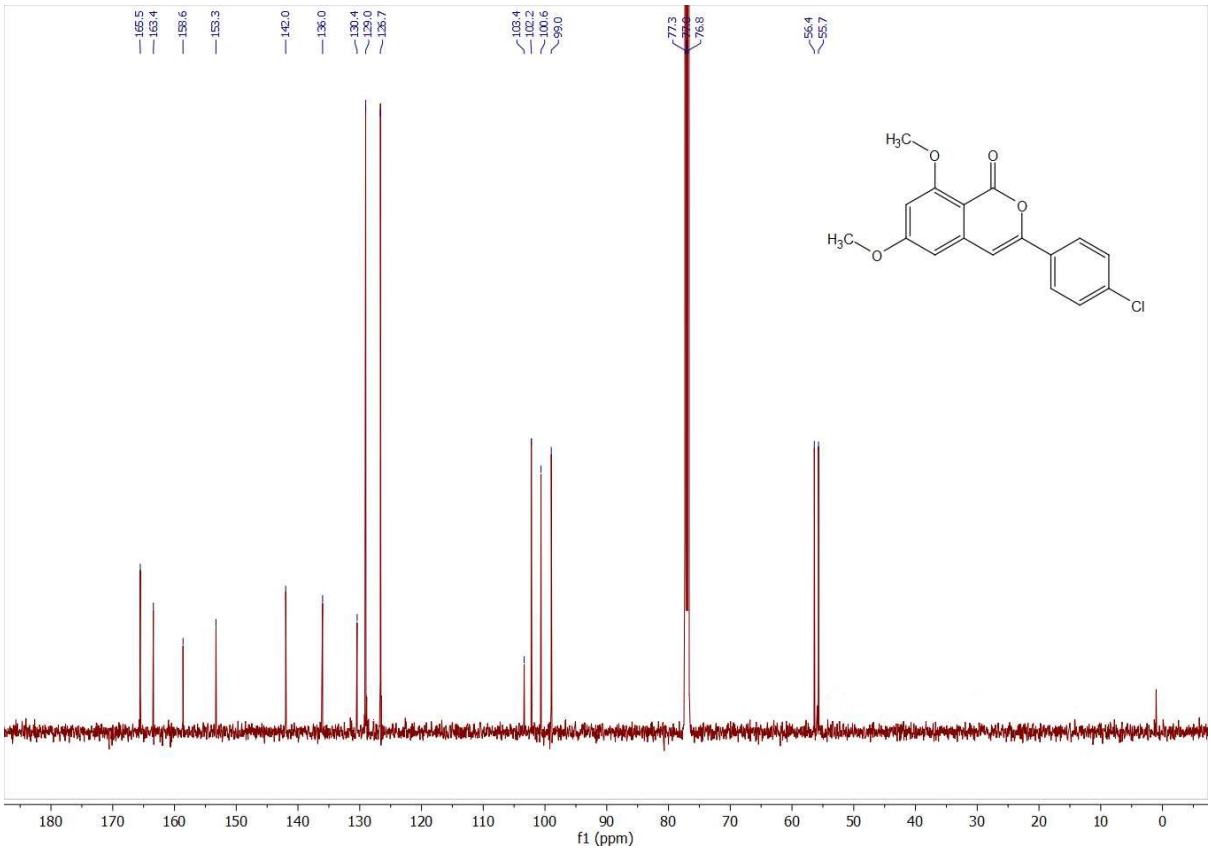
^{1}H NMR of compound 20



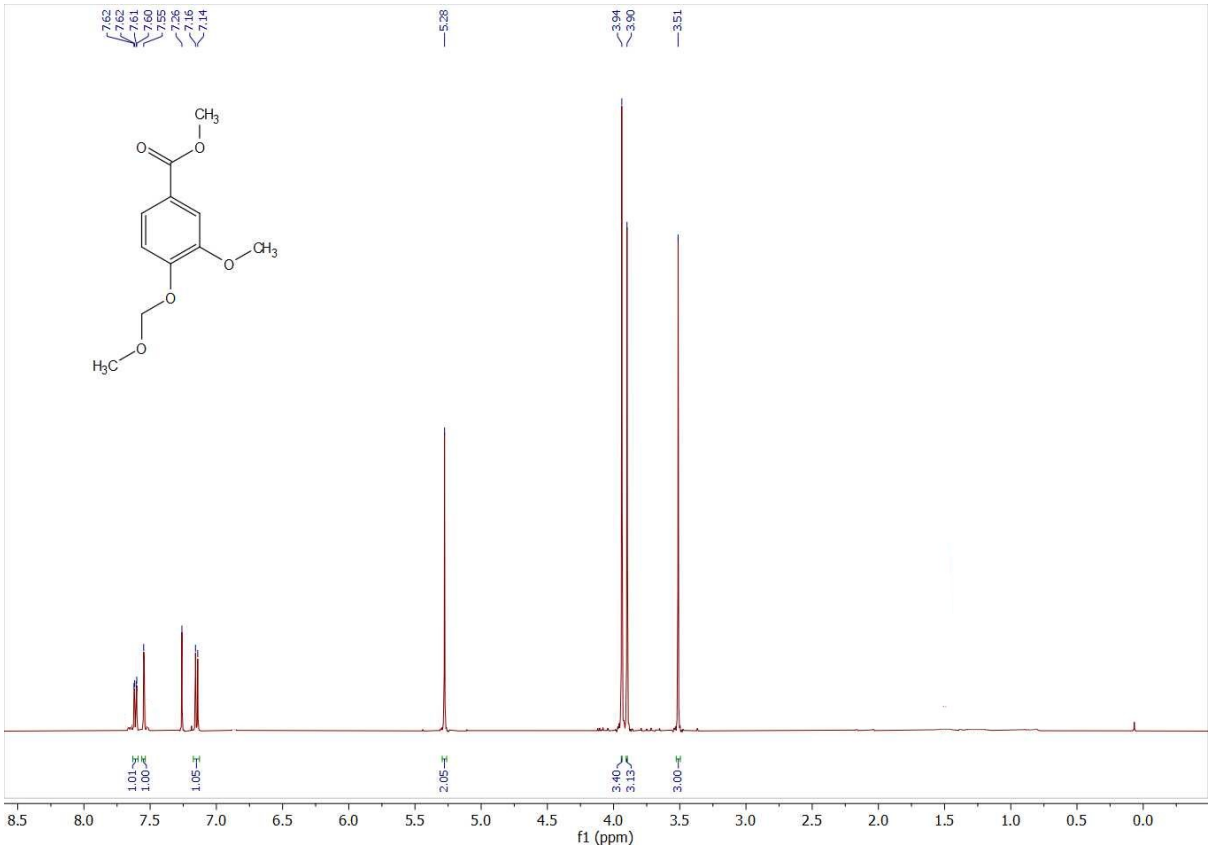
^{13}C{H} NMR of compound 20



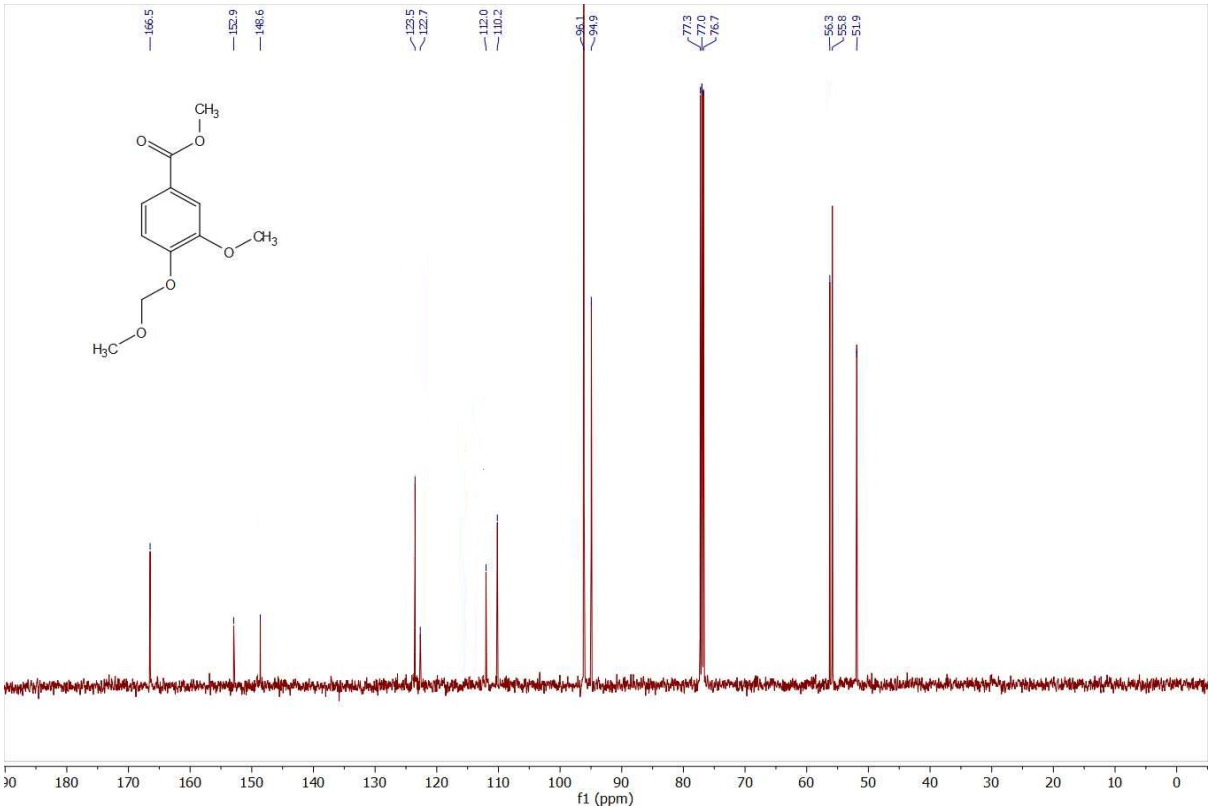
^{1}H NMR of compound 21



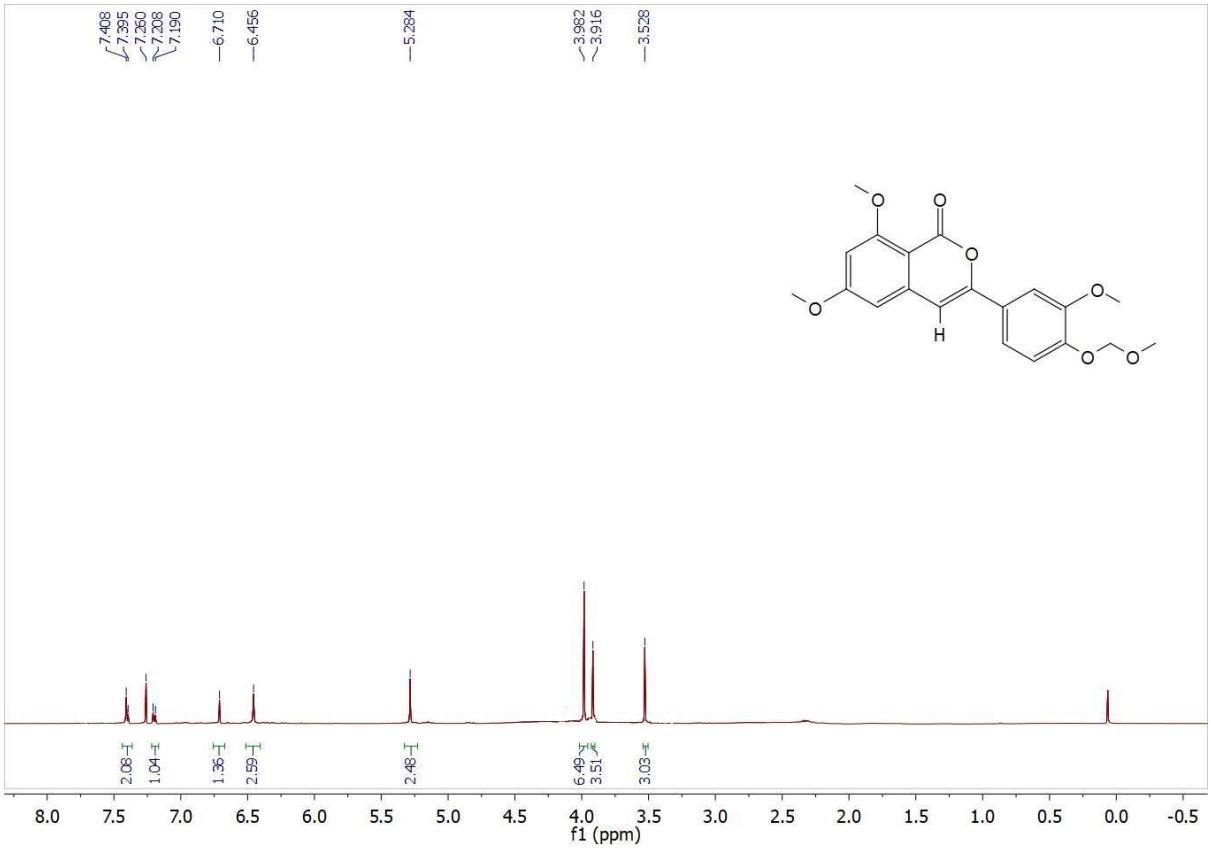
^{13}C{H} NMR of compound 21



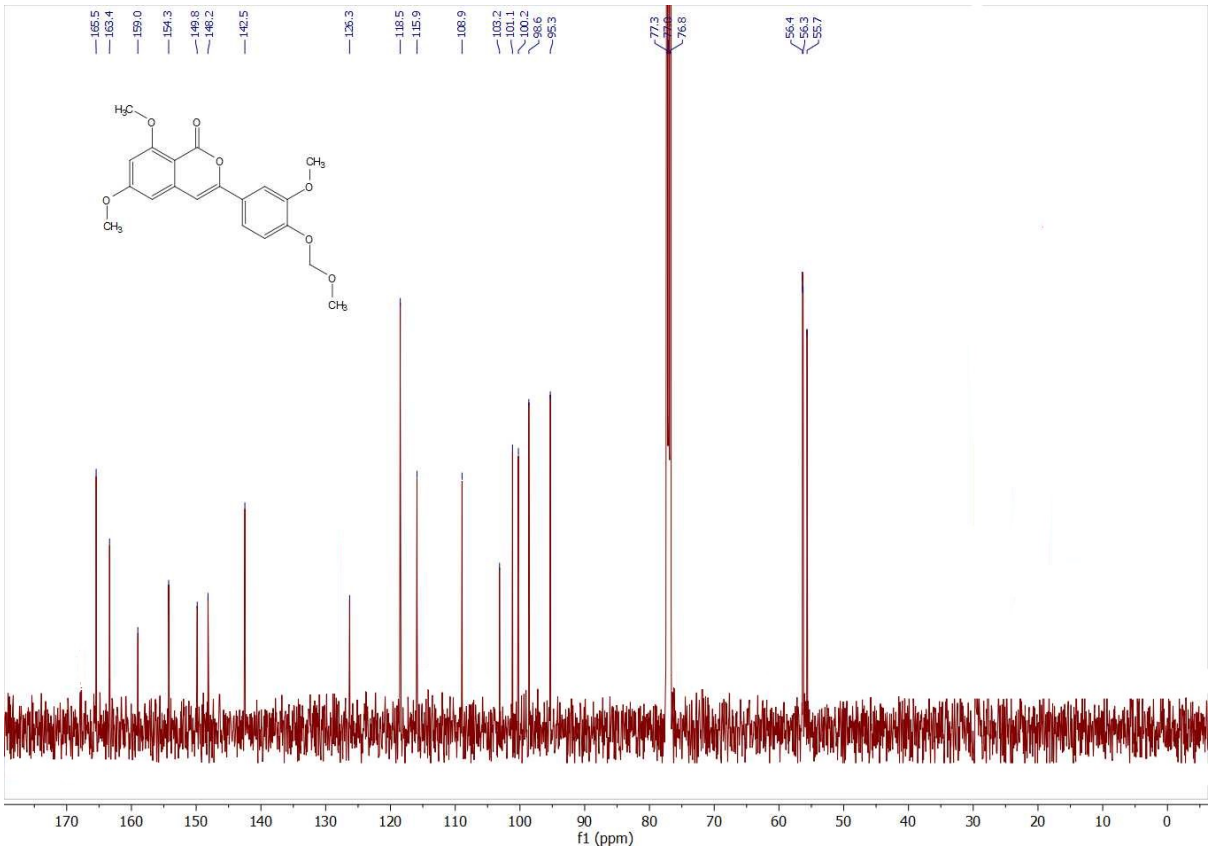
^{1}H NMR of compound 22a



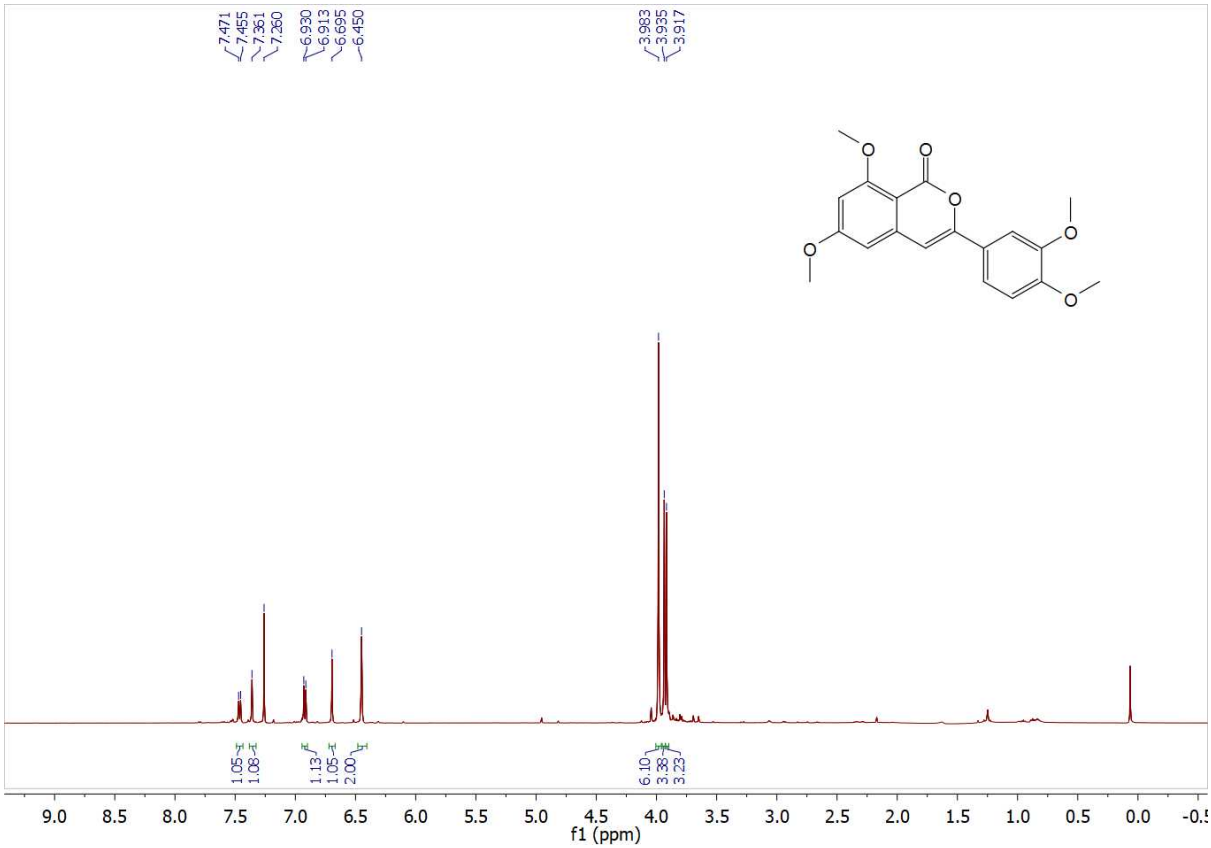
^{13}C{H} NMR of compound 22a



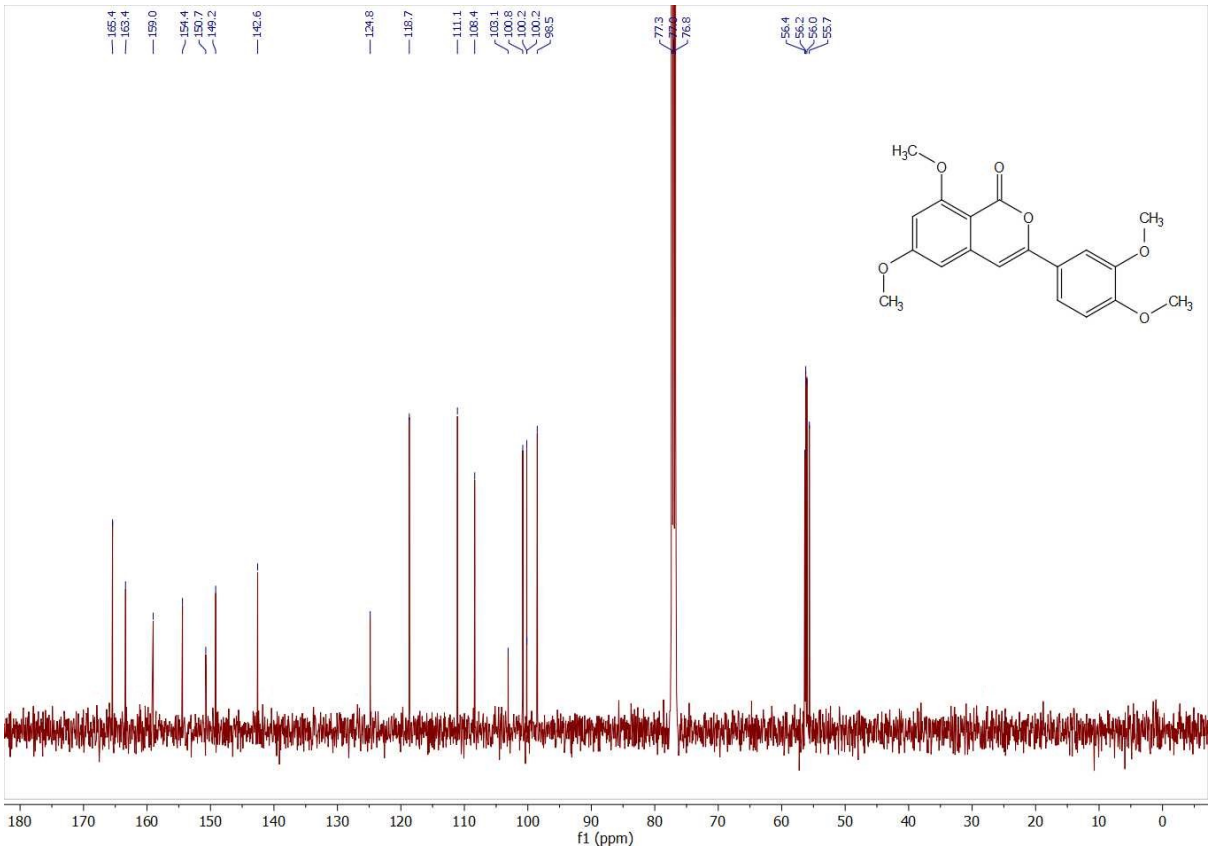
^{1}H NMR of compound 22



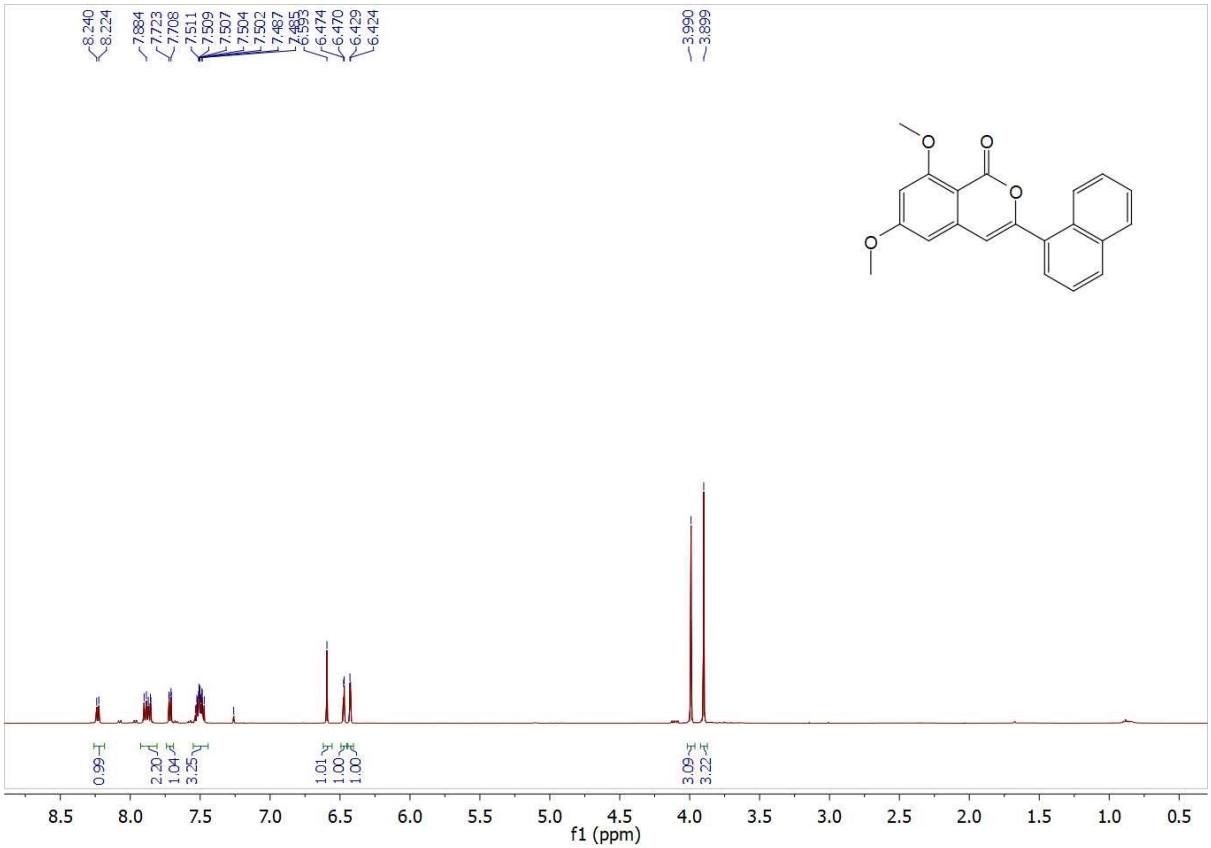
^{13}C{H} NMR of compound 22



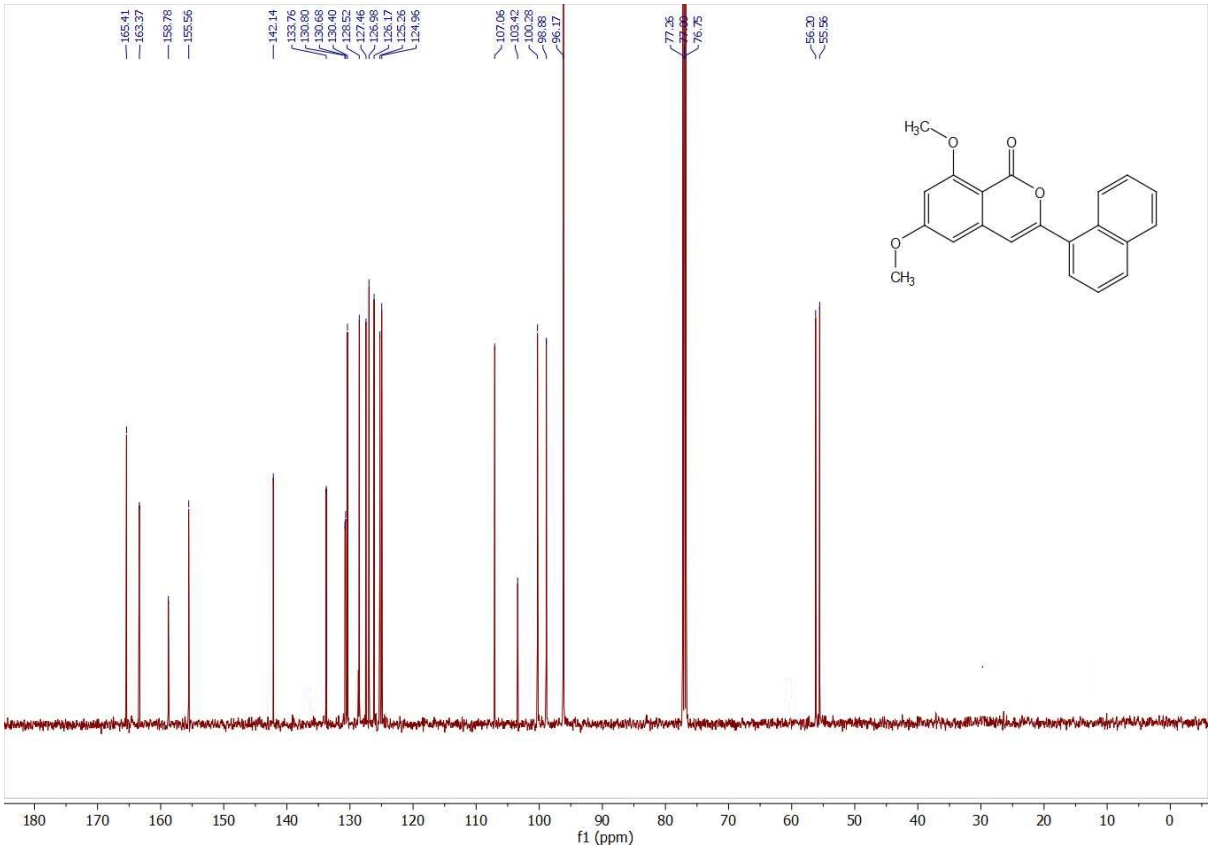
^{1}H NMR of compound 23



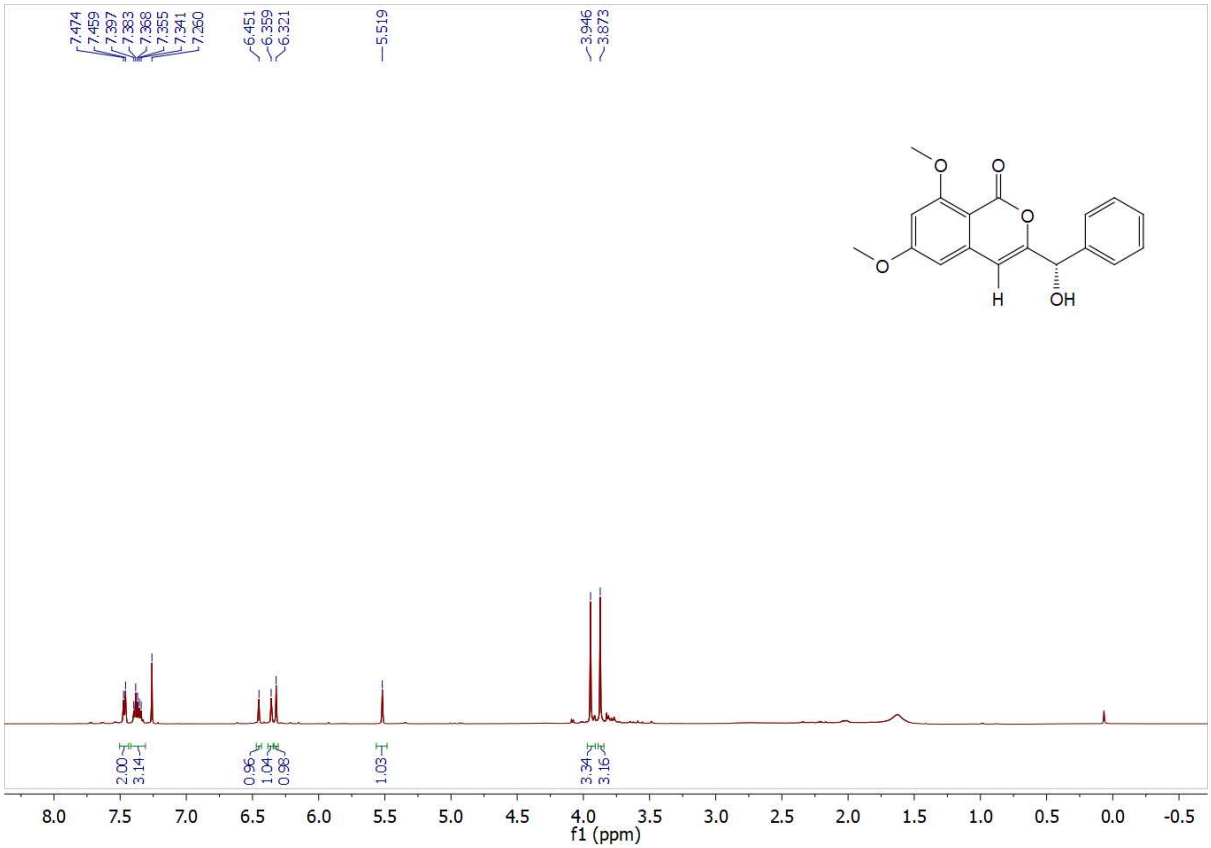
^{13}C{H} NMR of compound 23



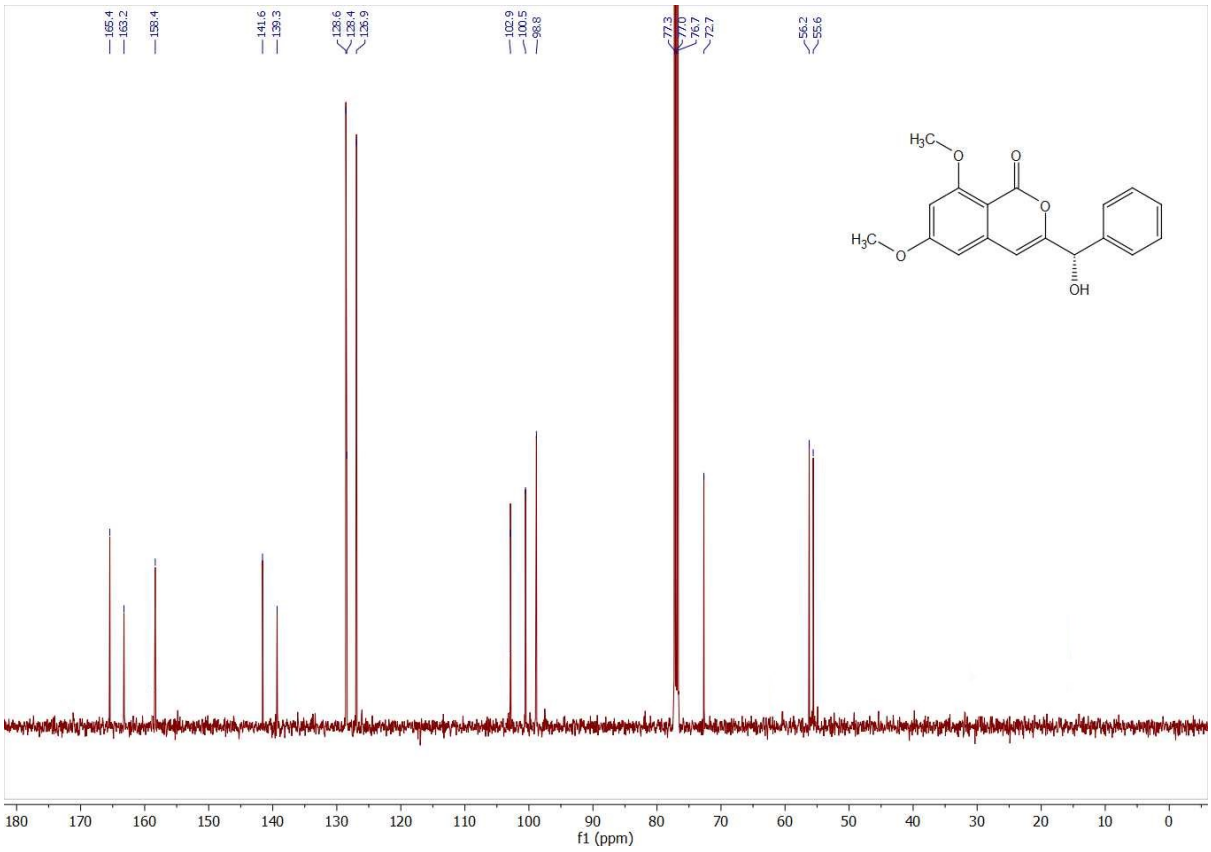
^{1}H NMR of compound 24



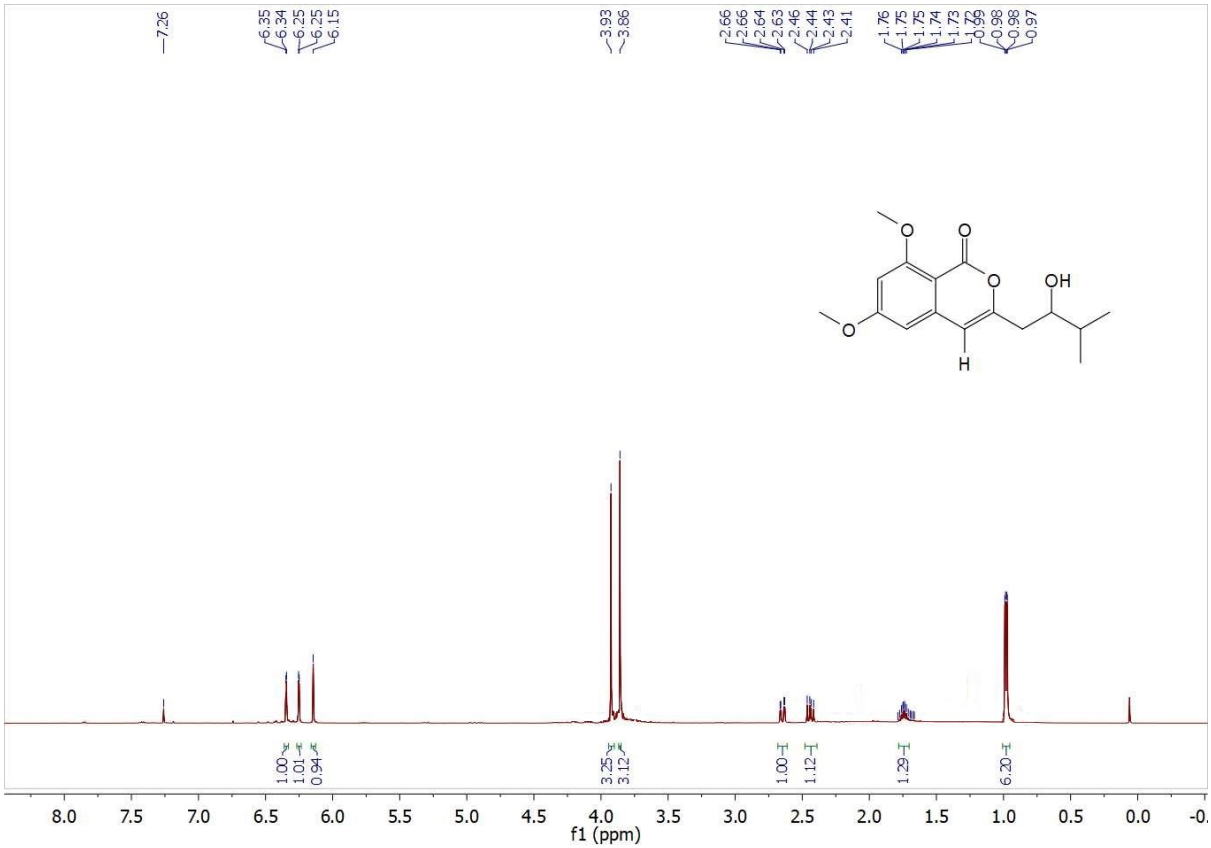
^{13}C{H} NMR of compound 24



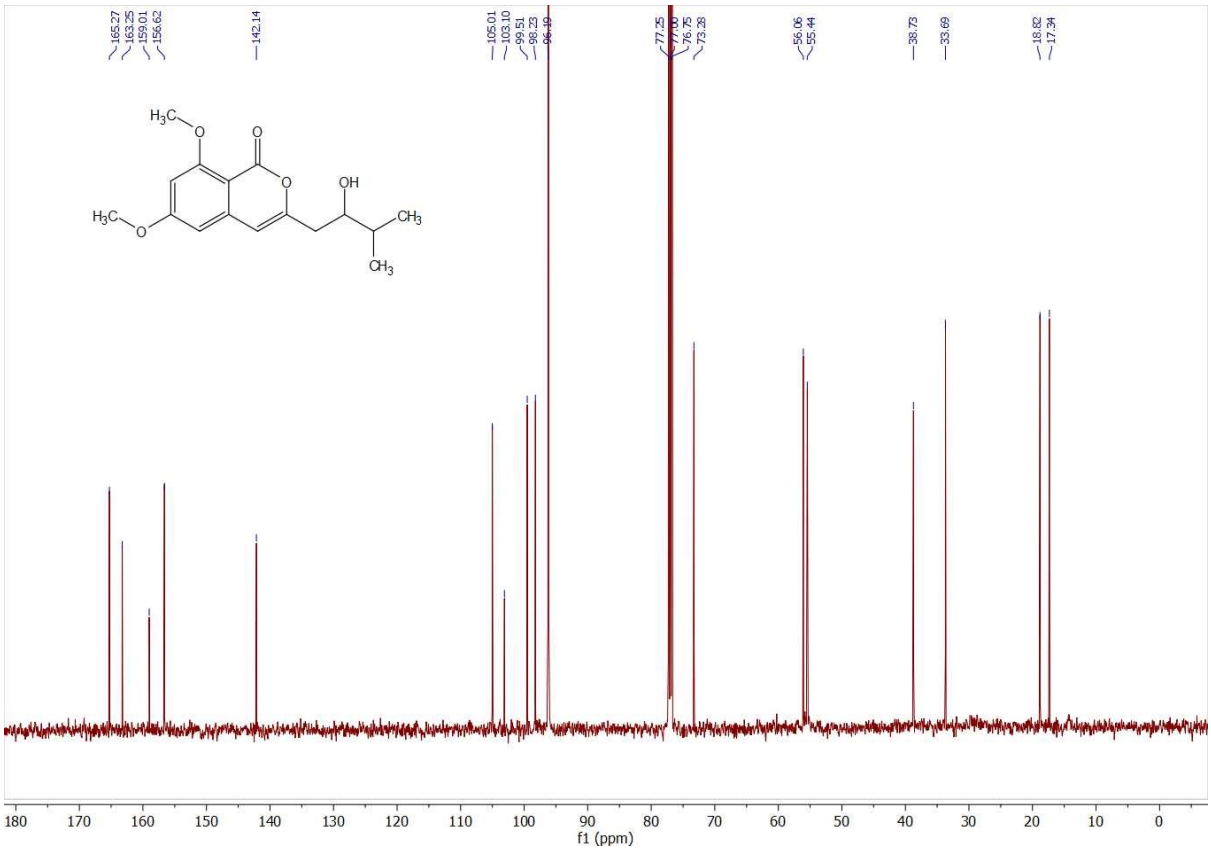
^{1}H NMR of compound 25



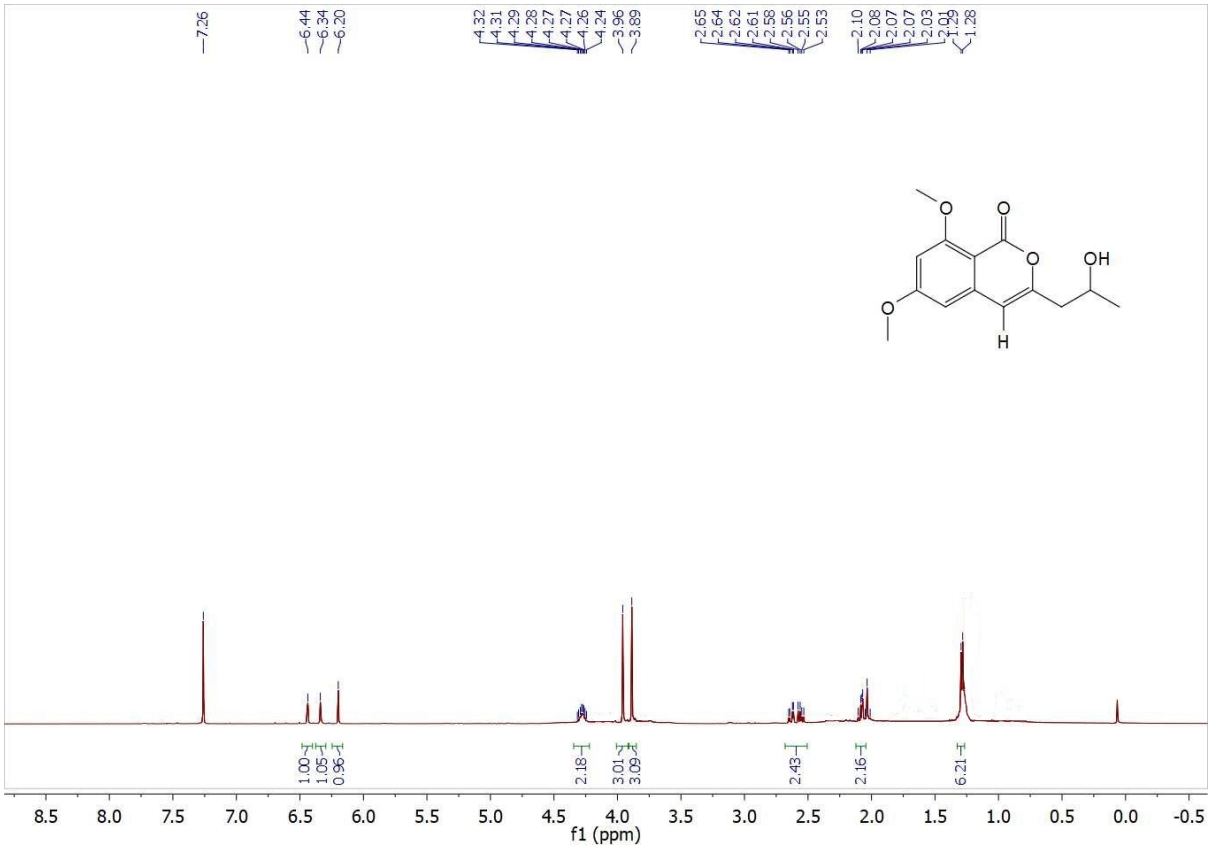
^{13}C{H} NMR of compound 25



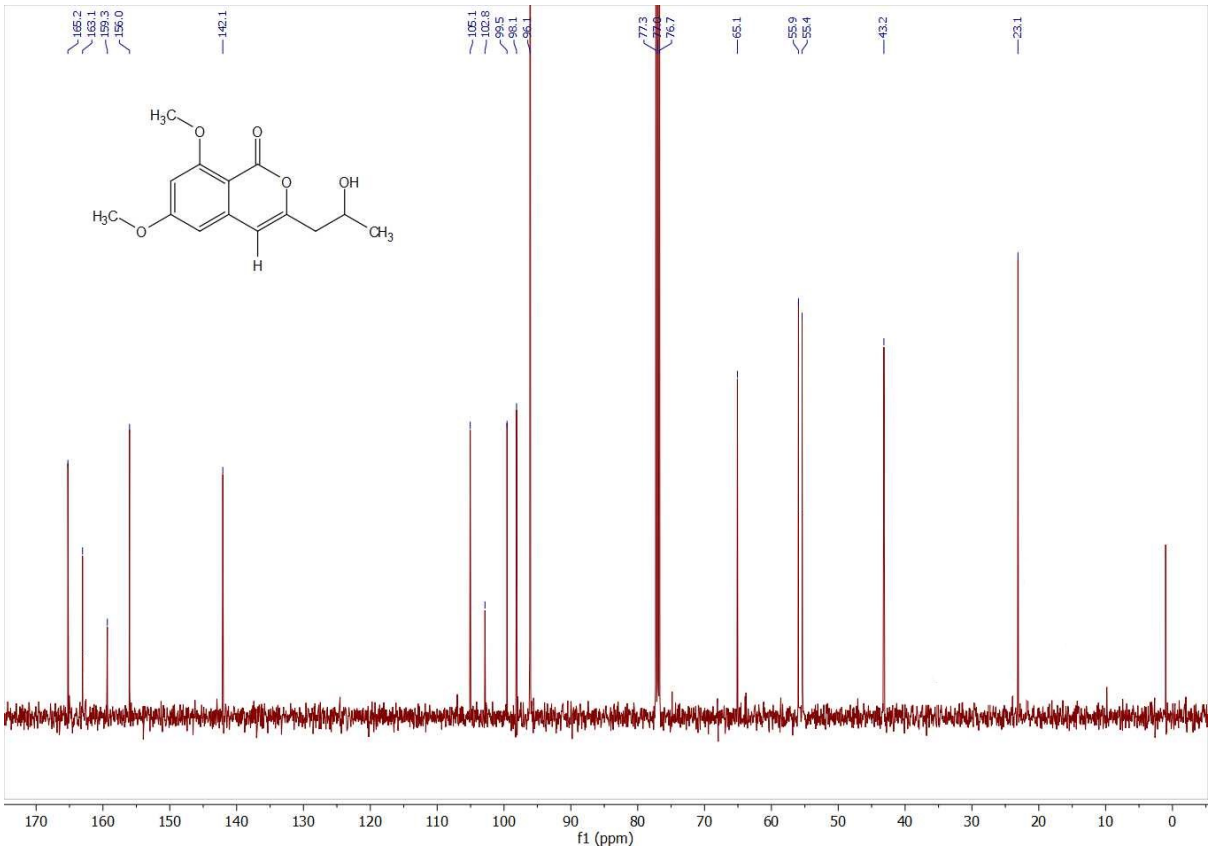
^{1}H NMR of compound 26



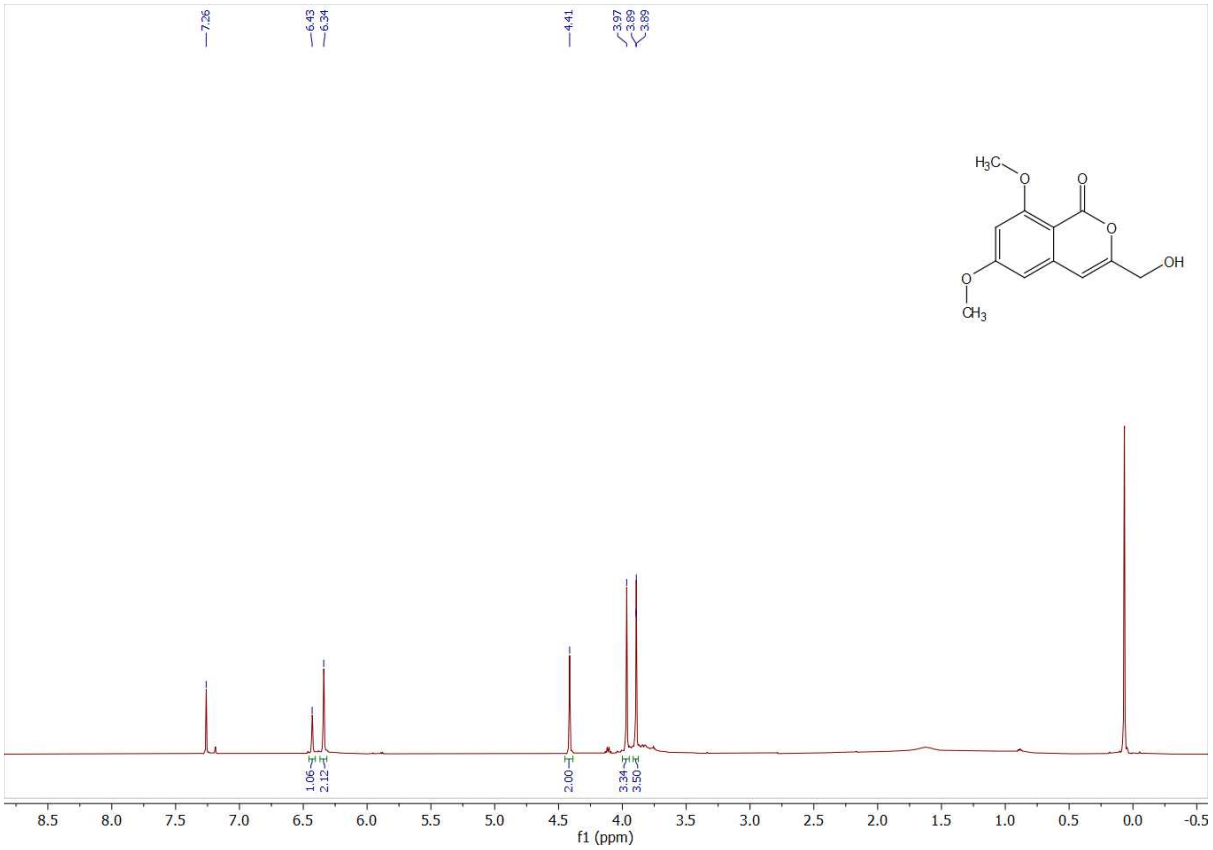
^{13}C{H} NMR of compound 26



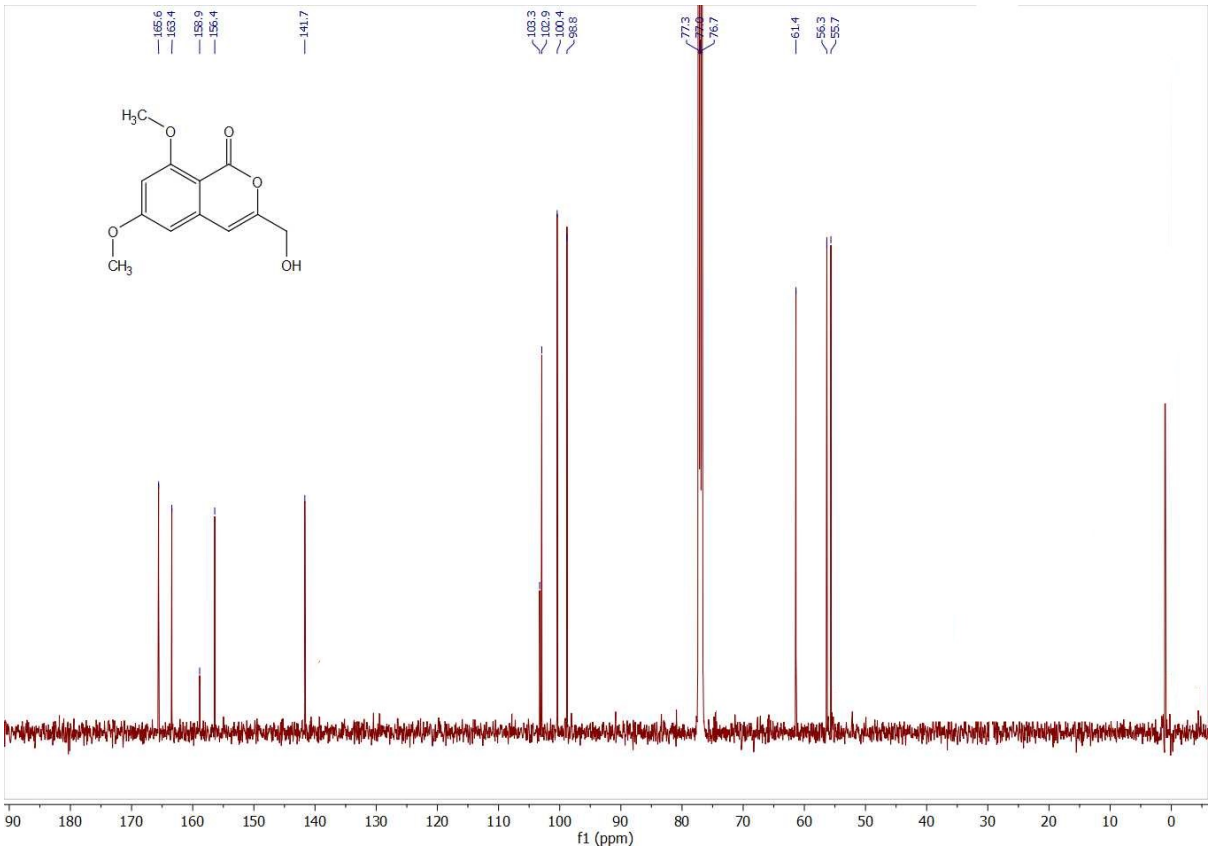
^{1}H NMR of compound 27



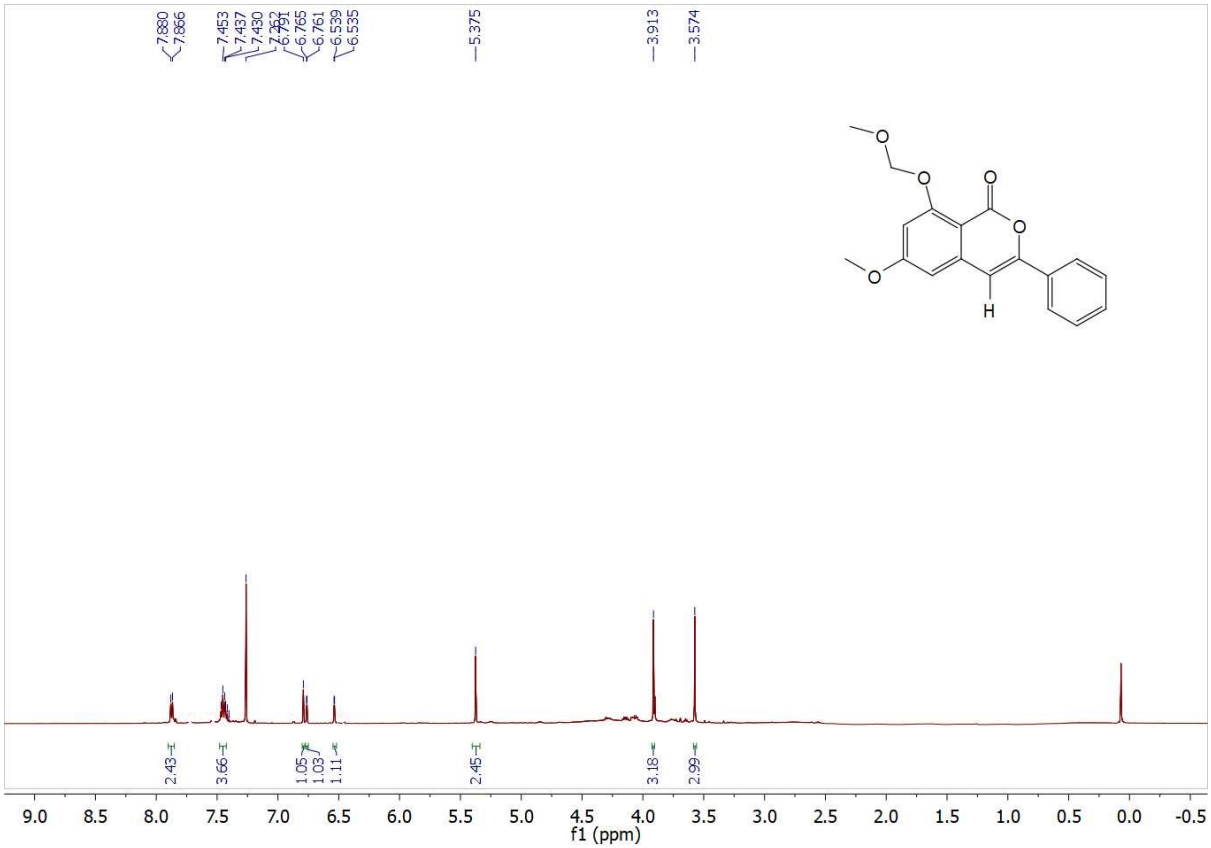
^{13}C{H} NMR of compound 27



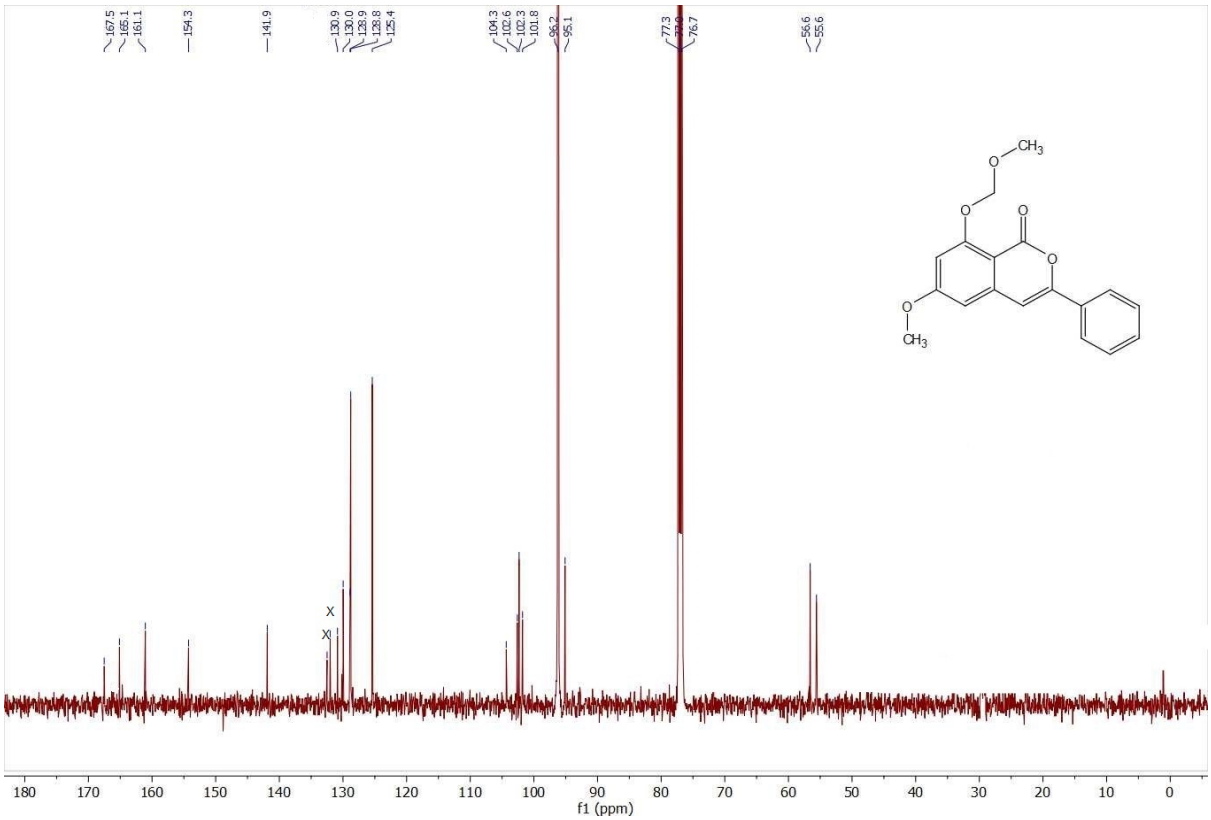
^{1}H NMR of Compound 28



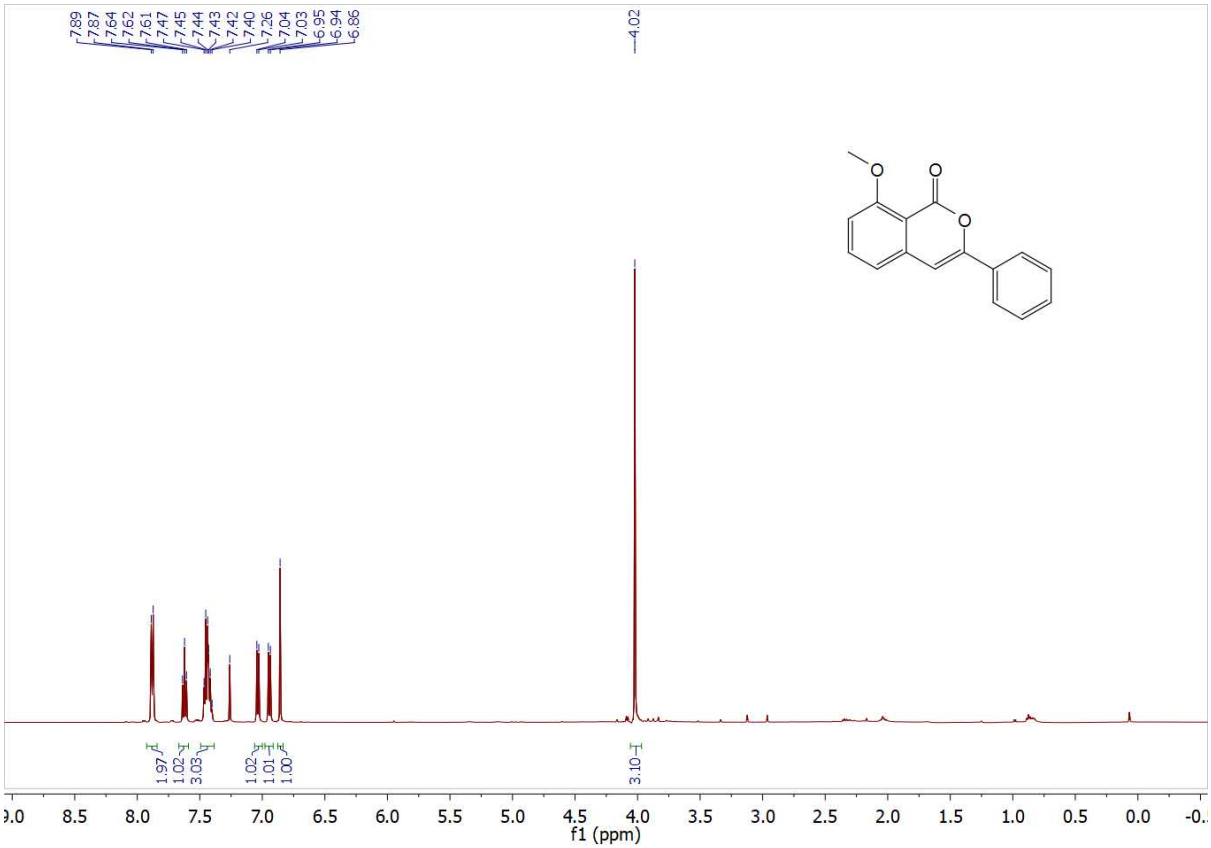
^{13}C{H} NMR of Compound 28



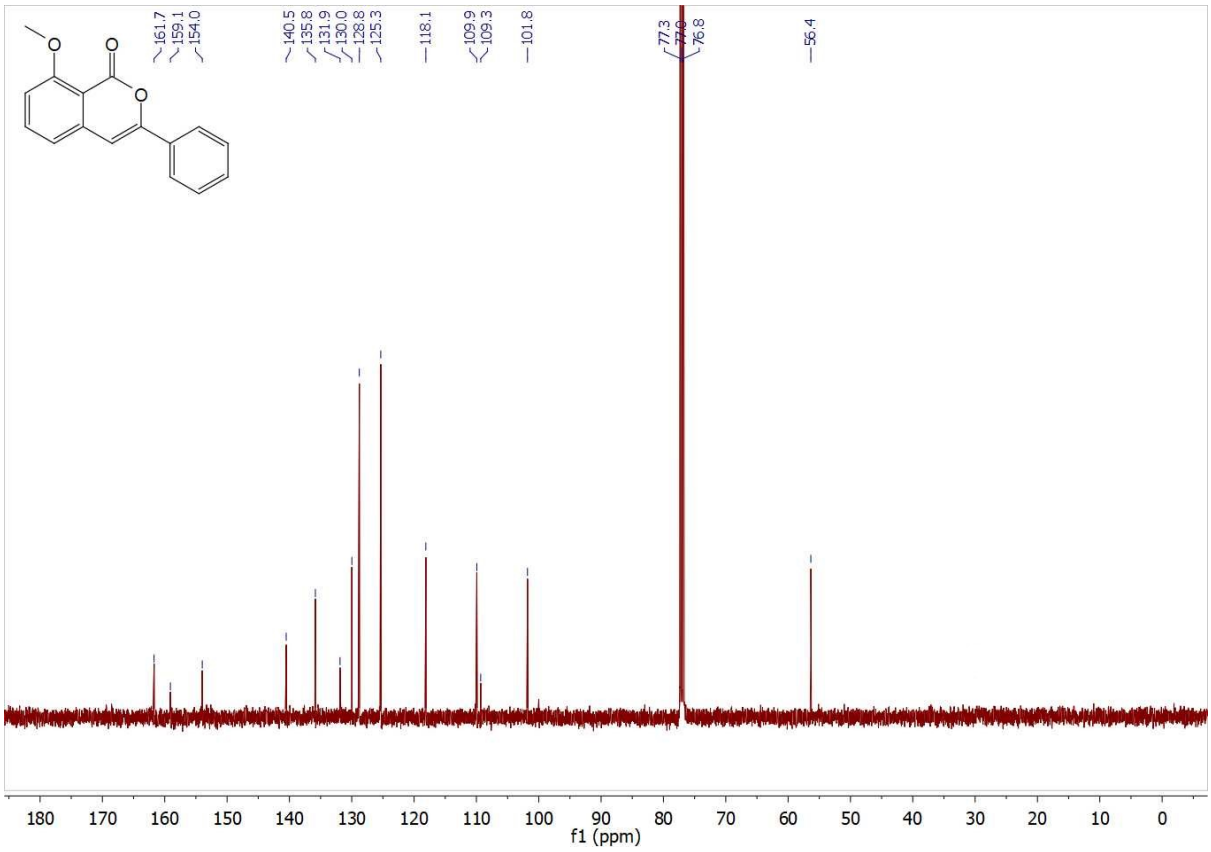
^{1}H NMR of compound 32



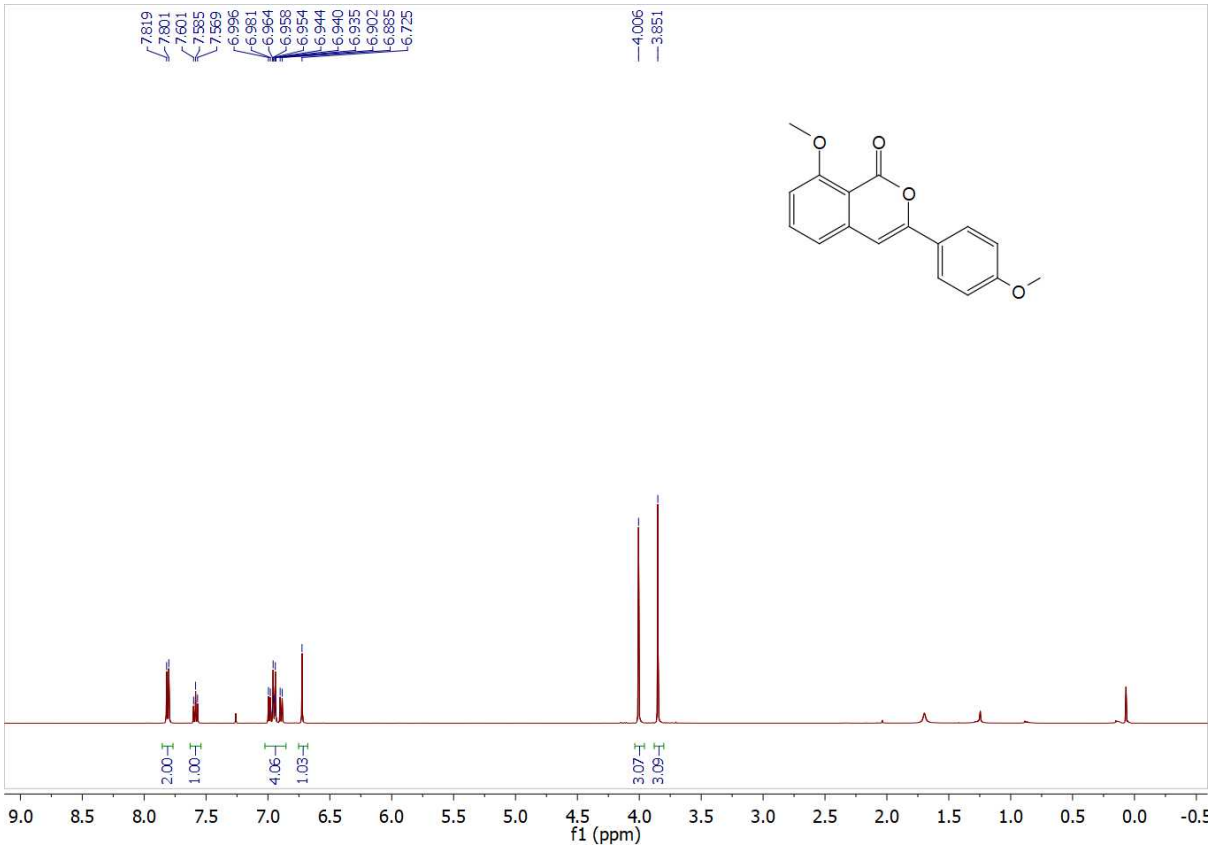
^{13}C{H} NMR of compound 32.



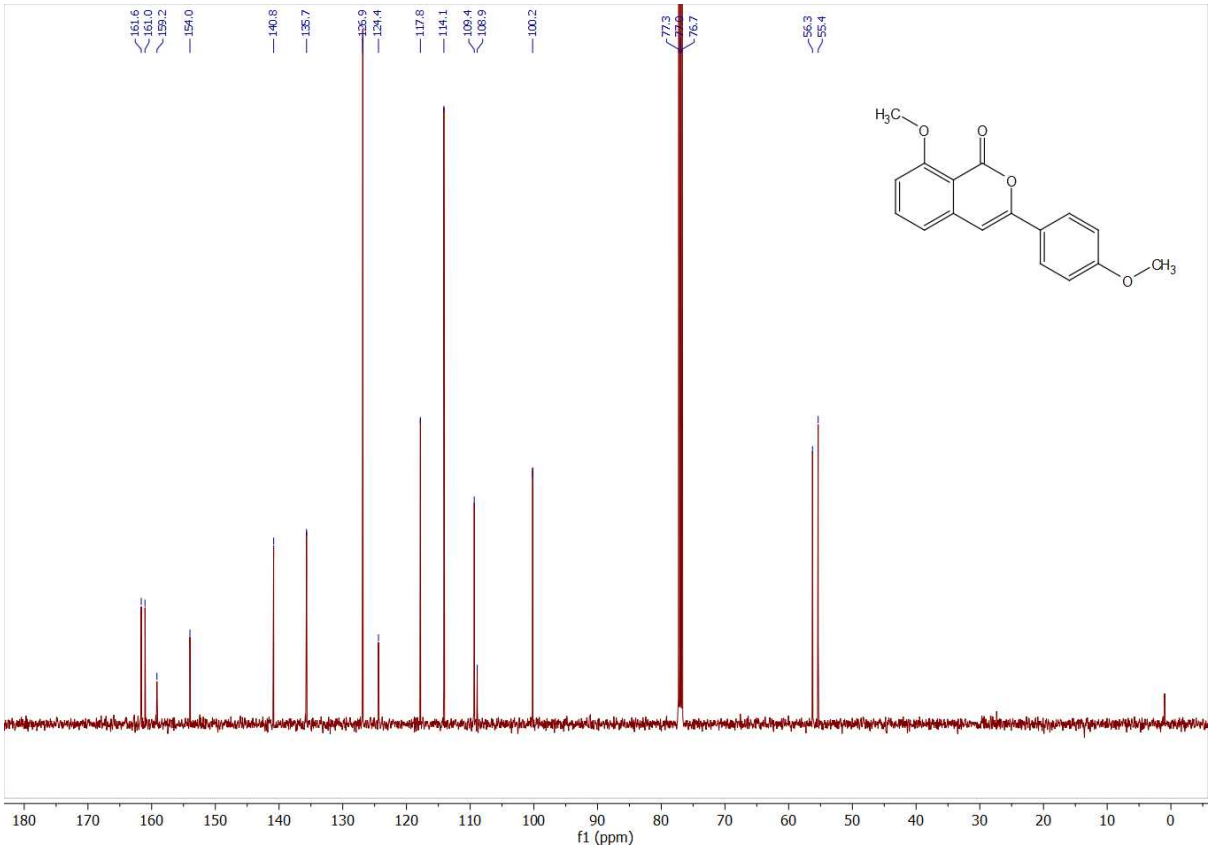
^{1}H NMR of compound 33



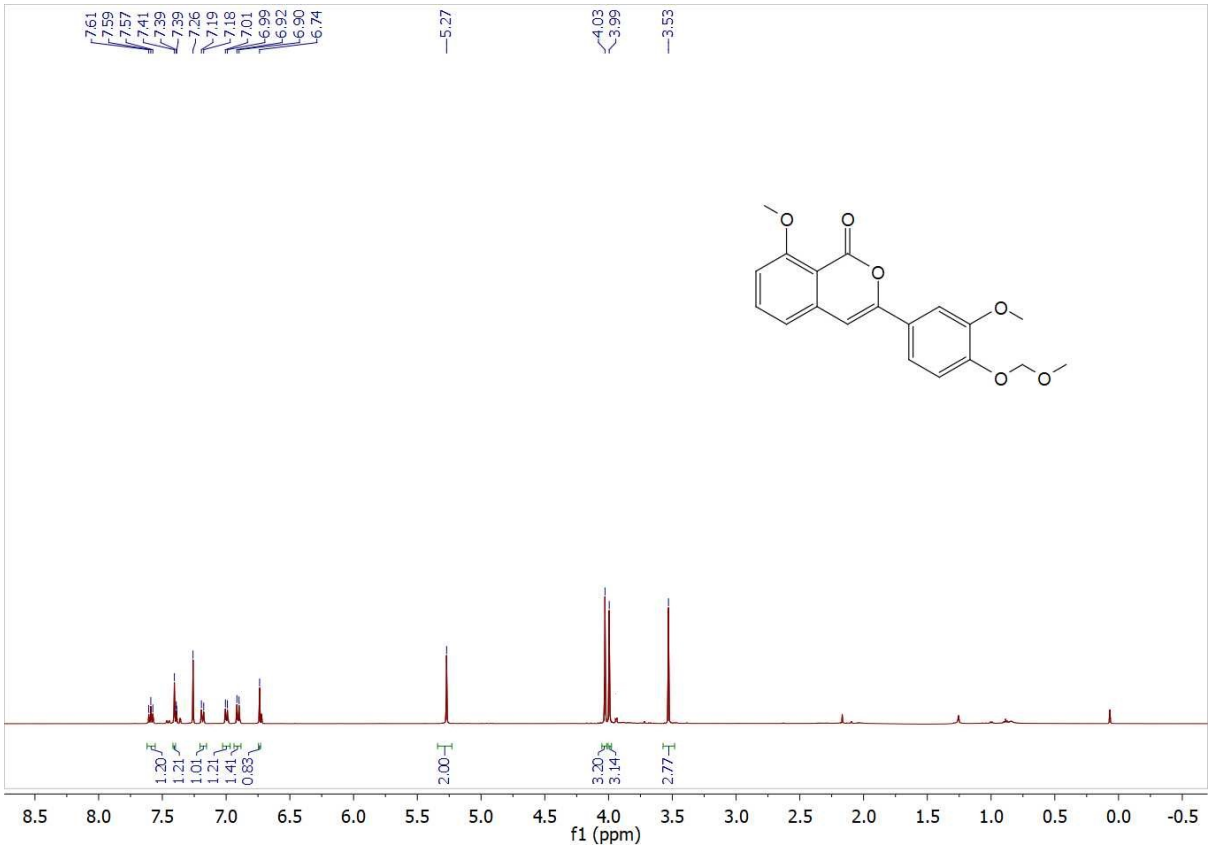
^{13}C{H} NMR of compound 33



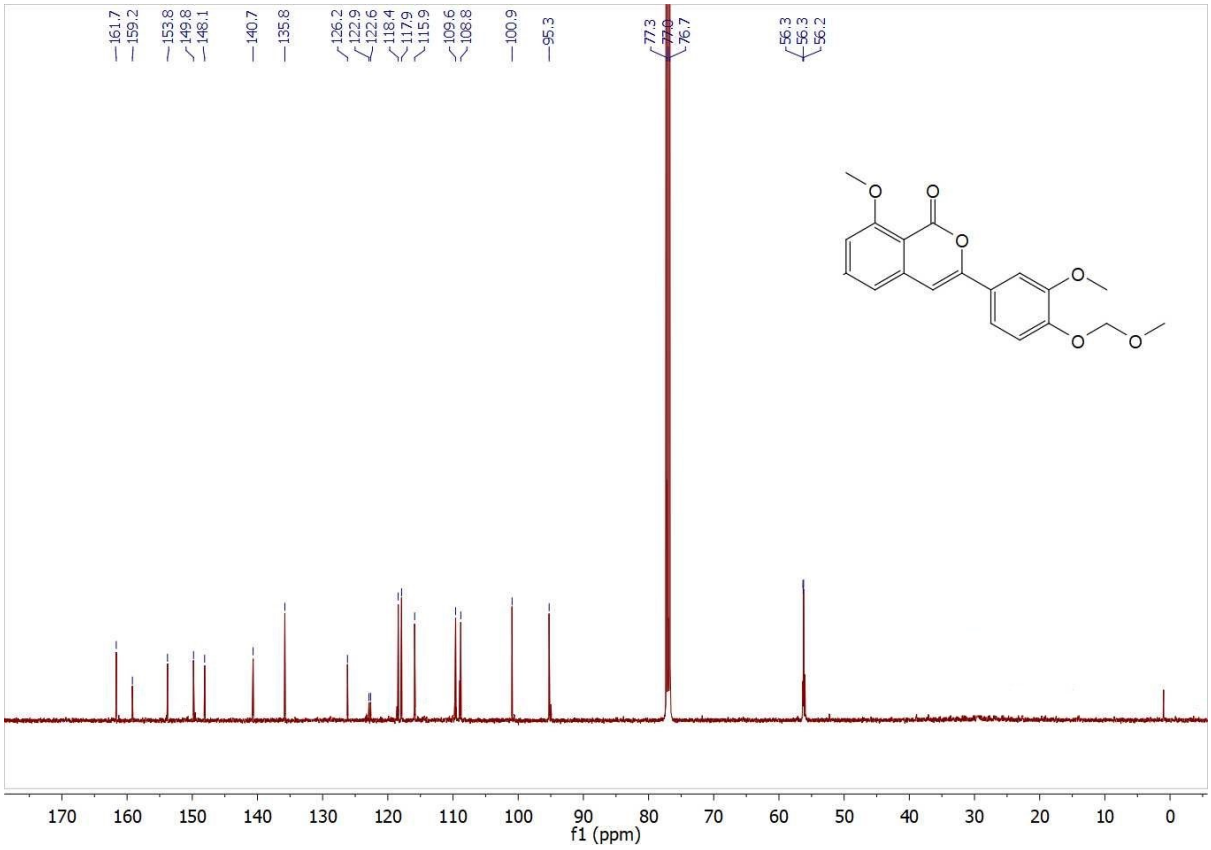
^{1}H NMR of compound 34



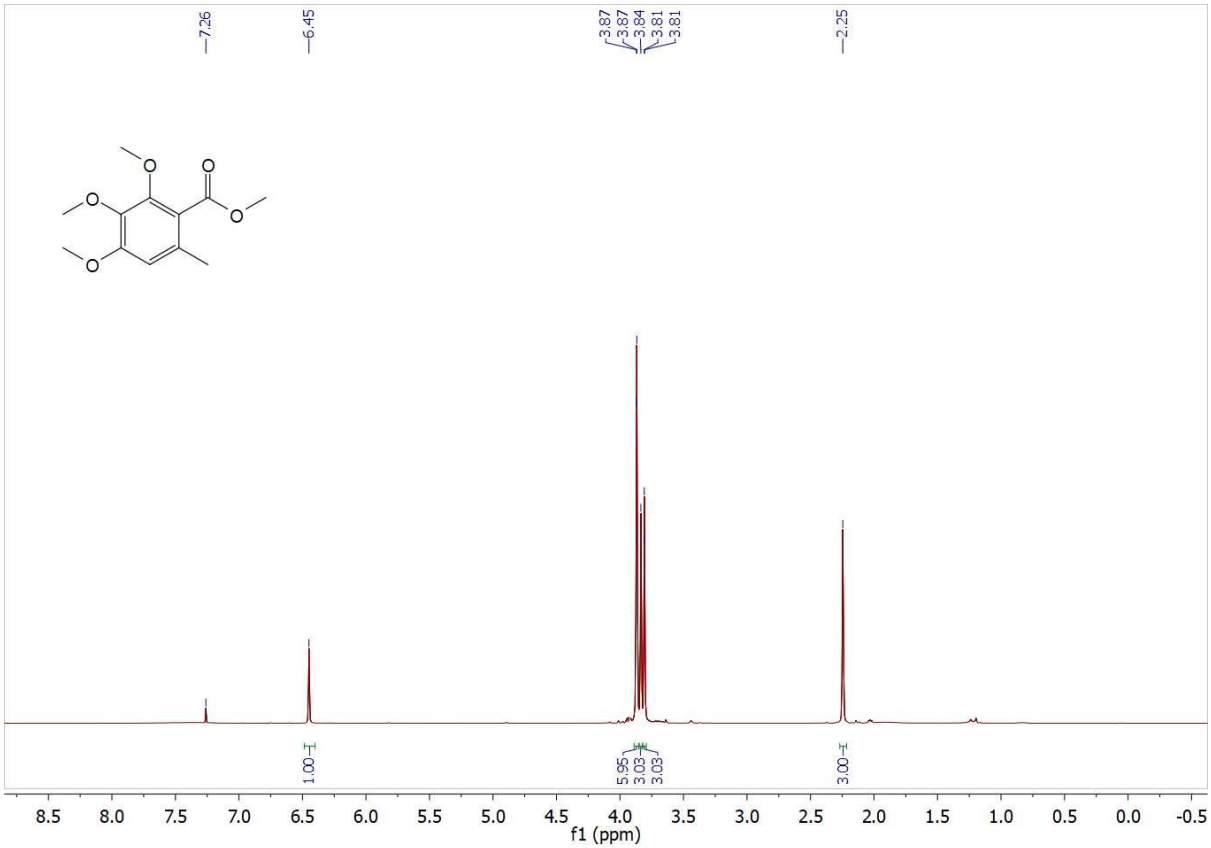
^{13}C{H}NMR of compound 34



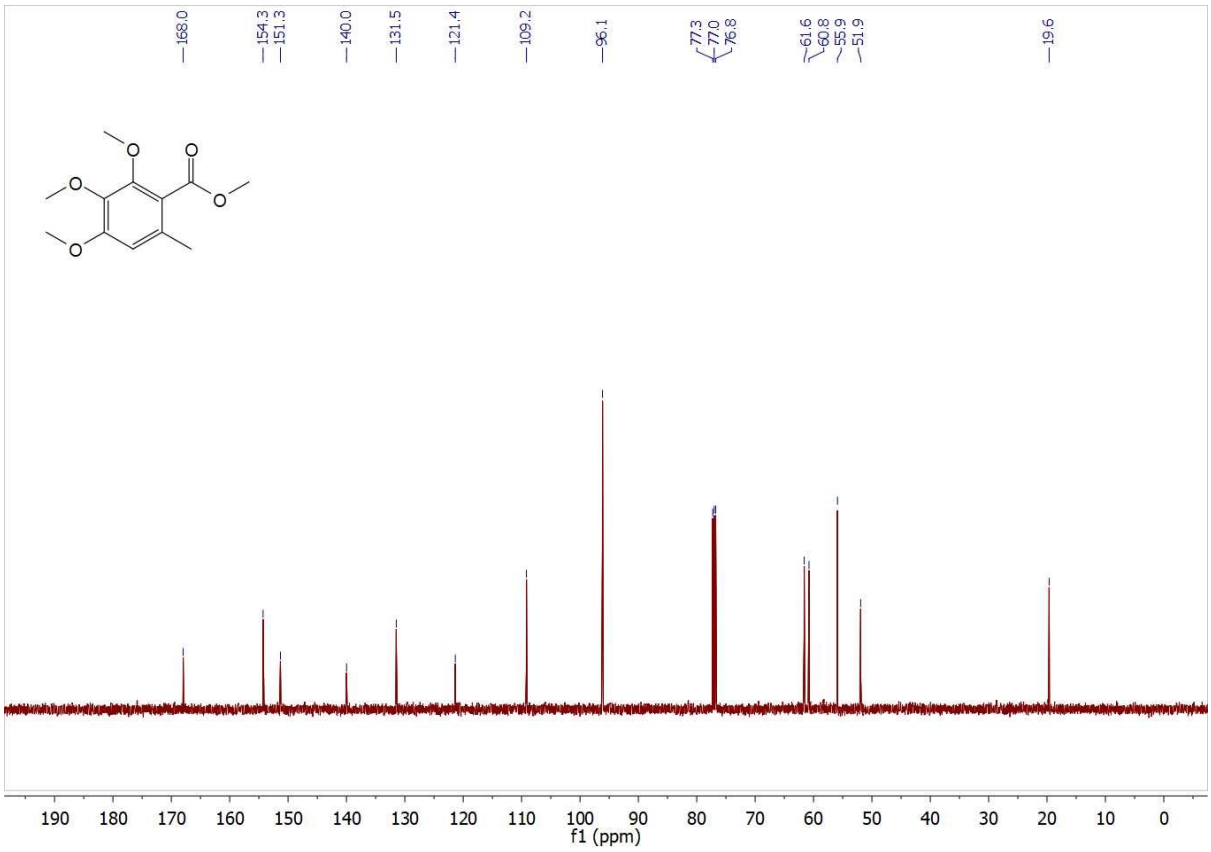
^{1}H NMR of compound 35



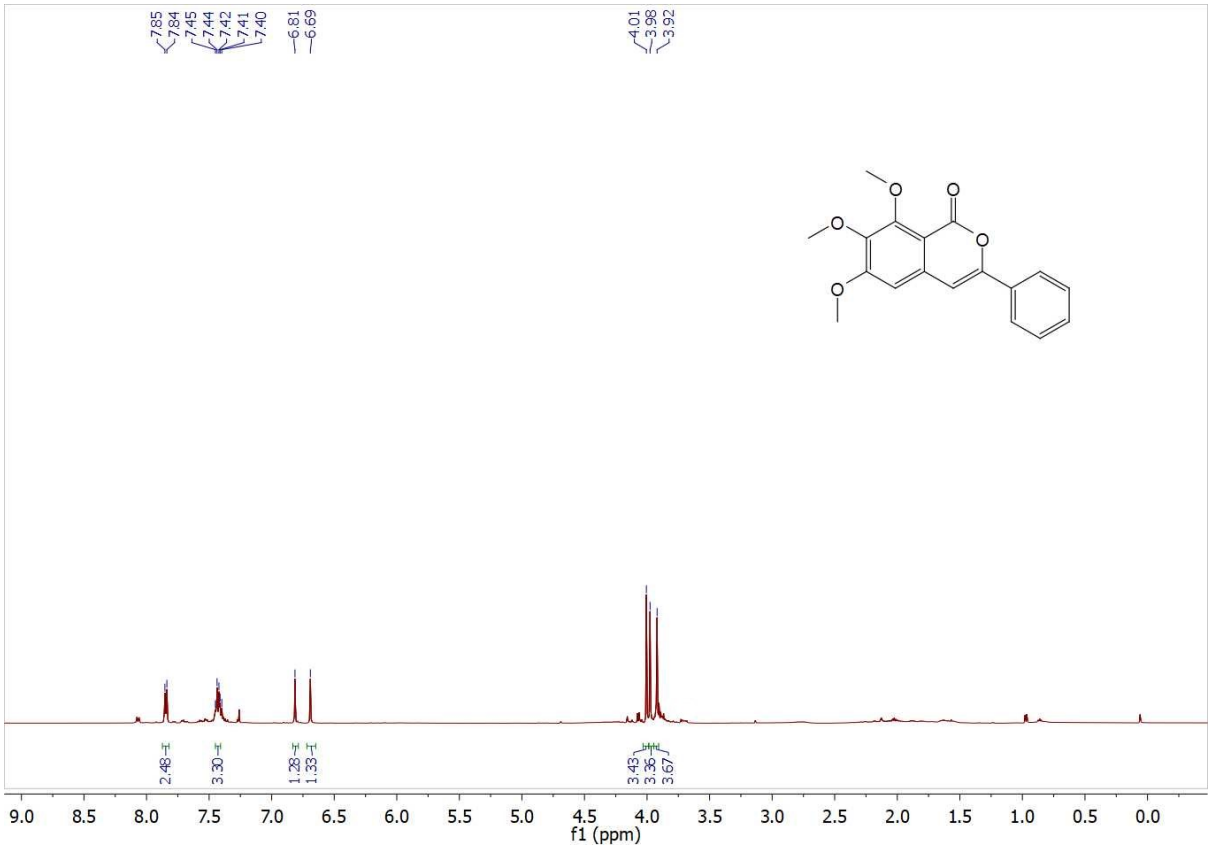
^{13}C{H} NMR of compound 35



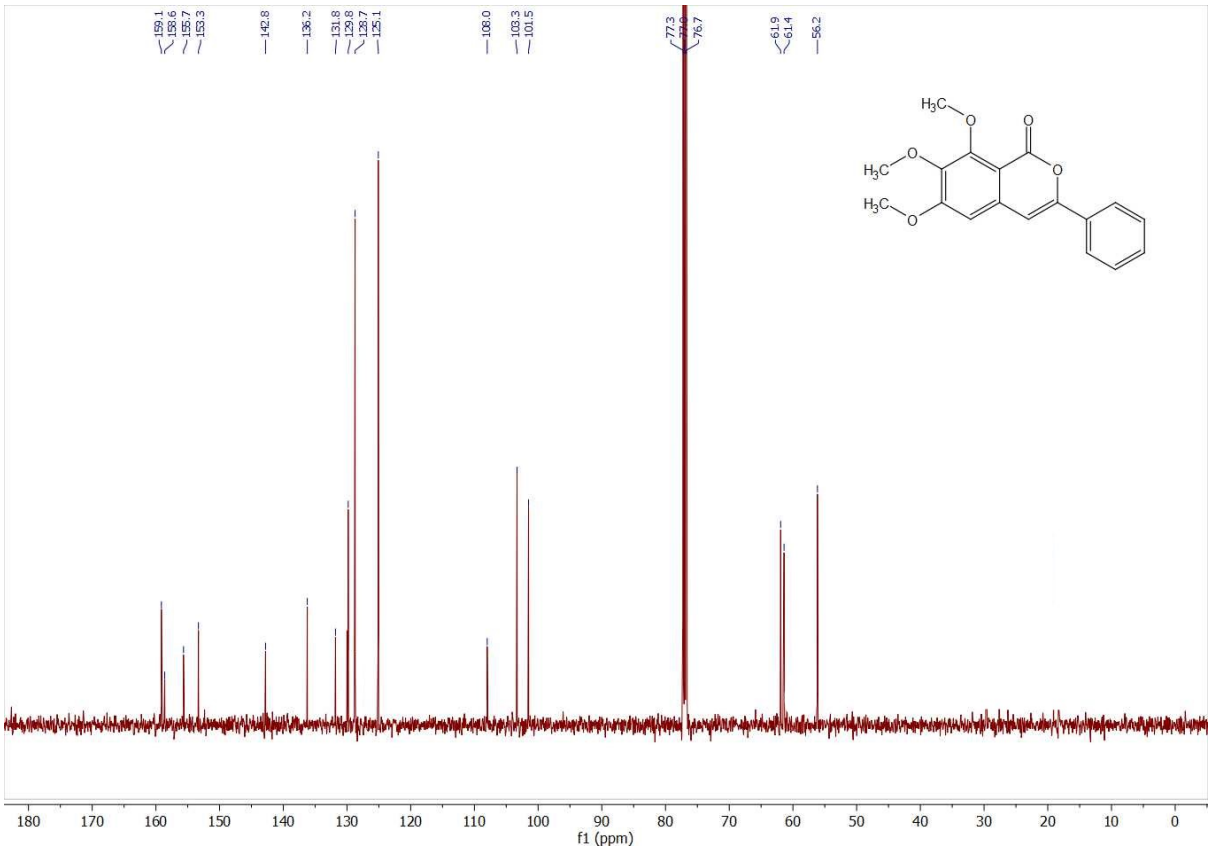
^{1}H NMR of compound 36a



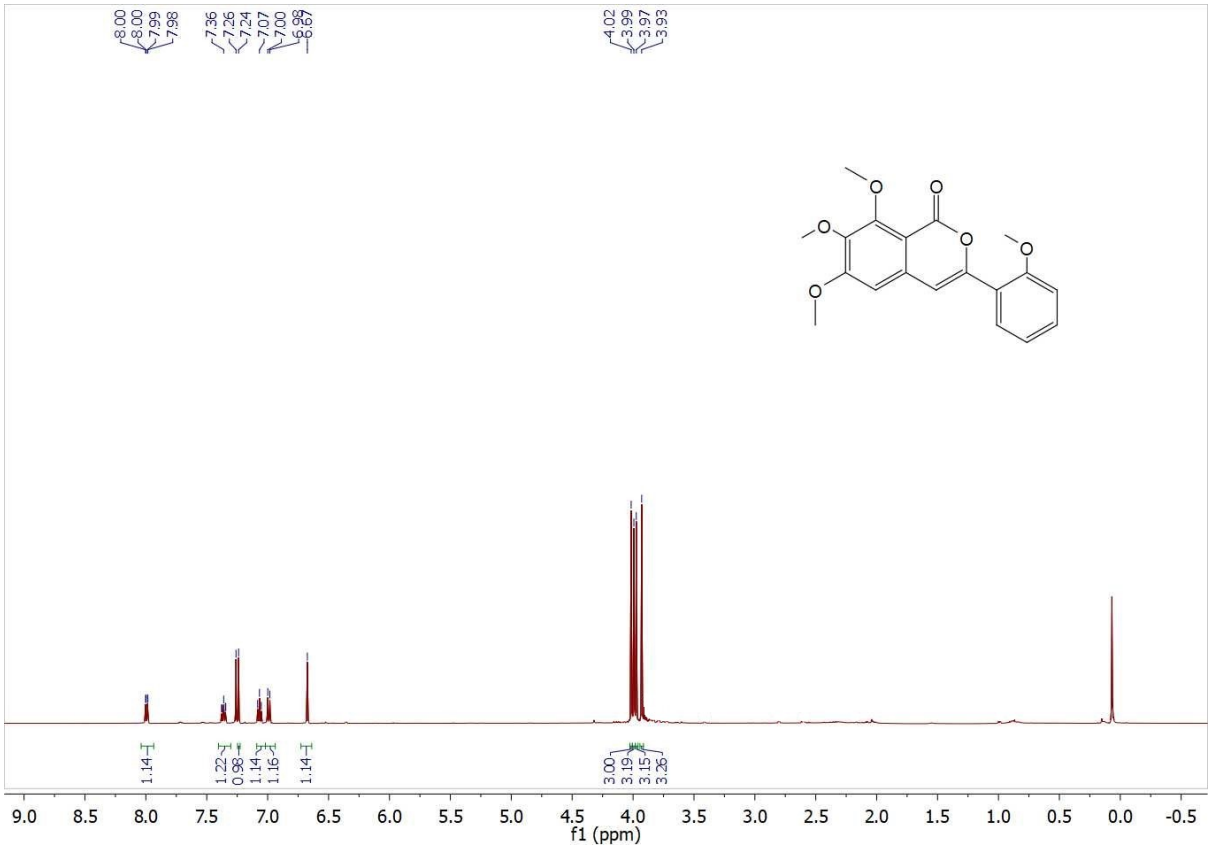
^{13}C{H} NMR of compound 36a



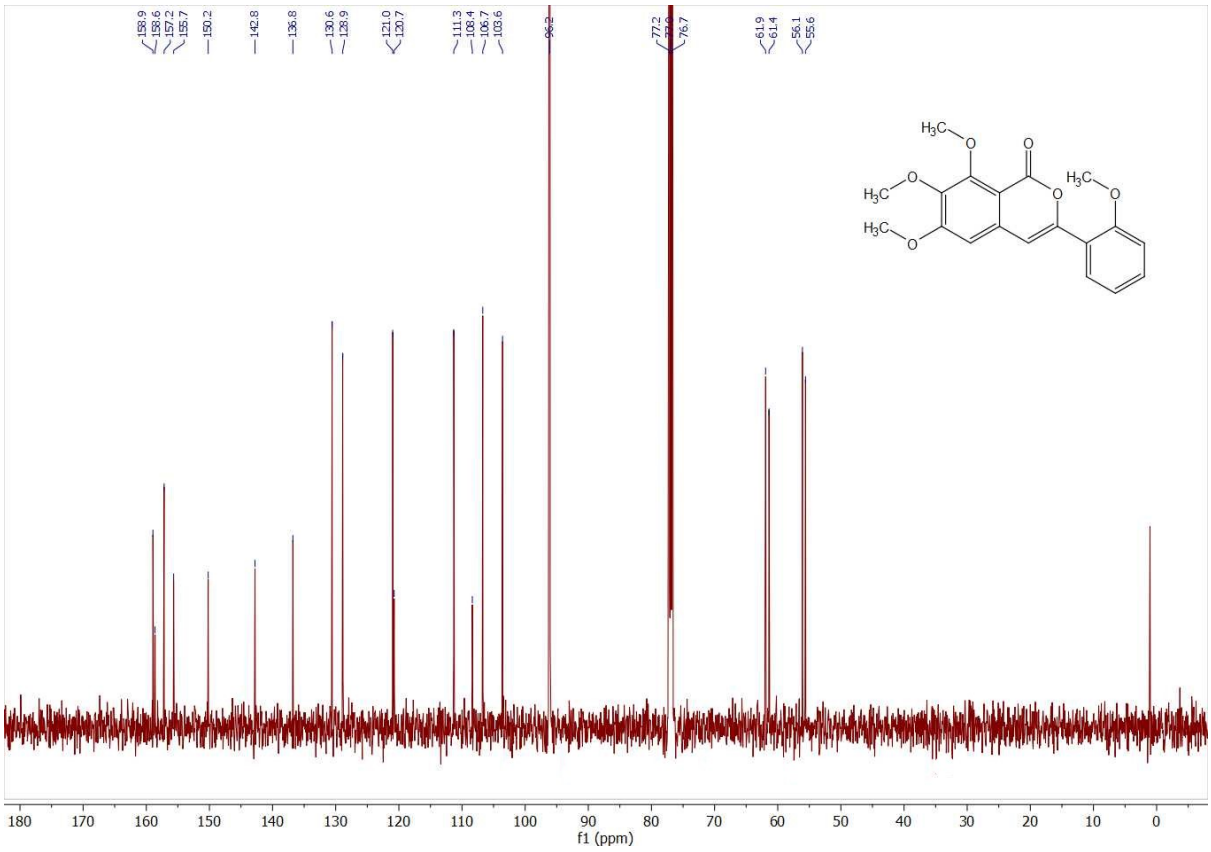
^{1}H NMR of compound 36



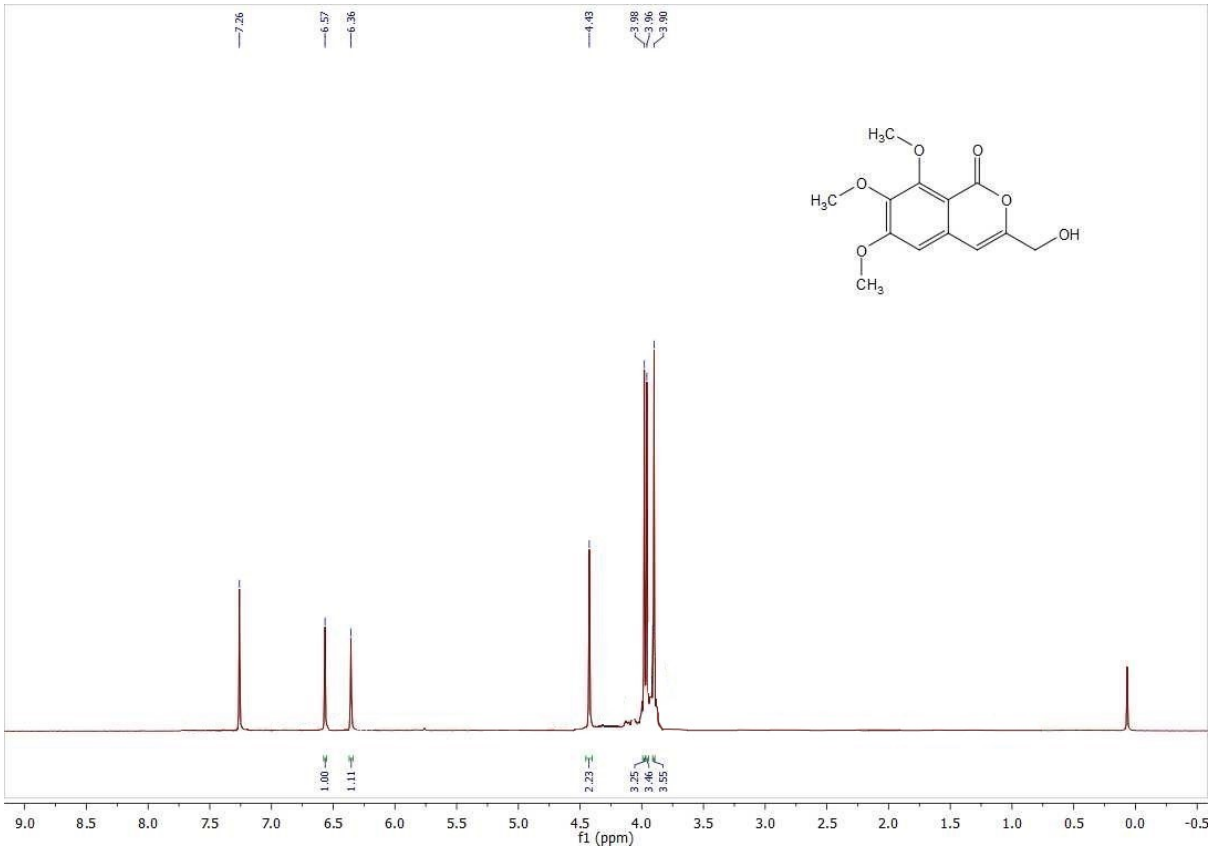
^{13}C{H} NMR of compound 36



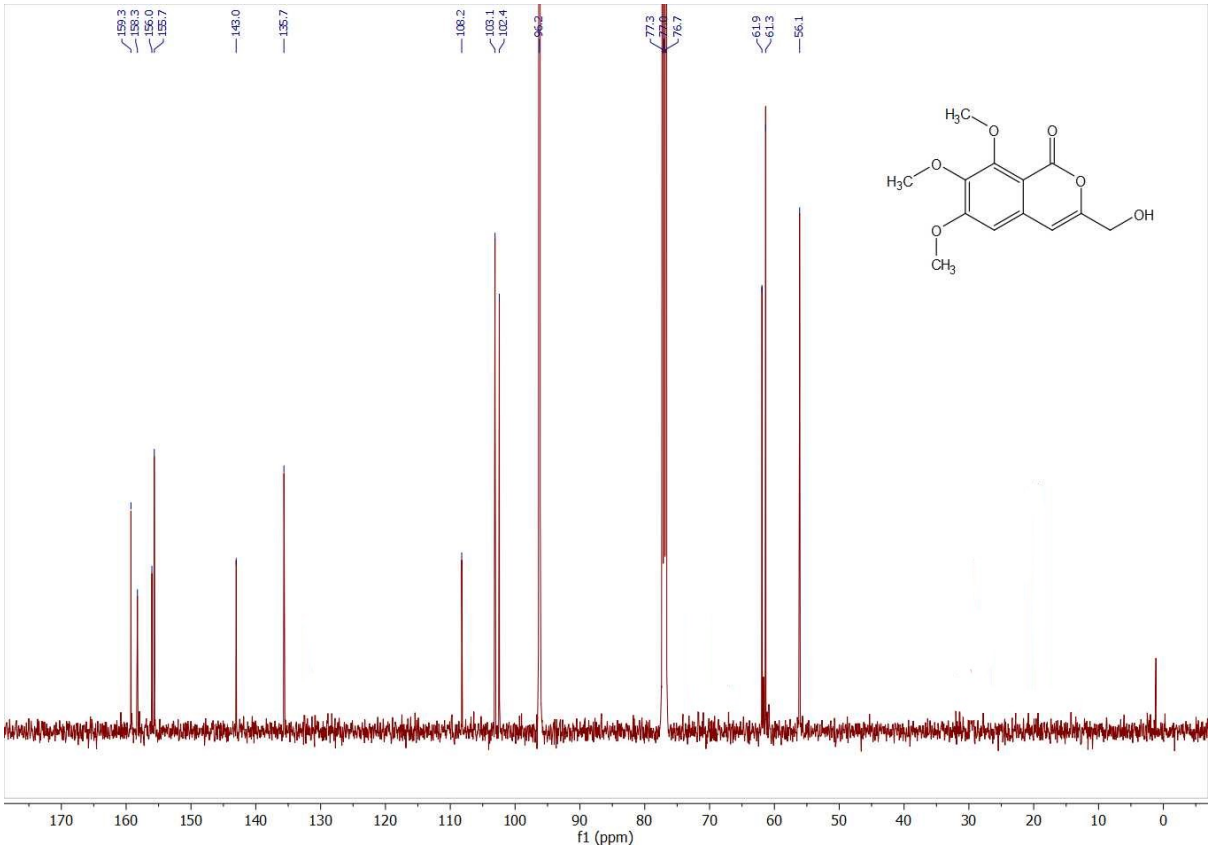
^{1}H NMR of compound 37



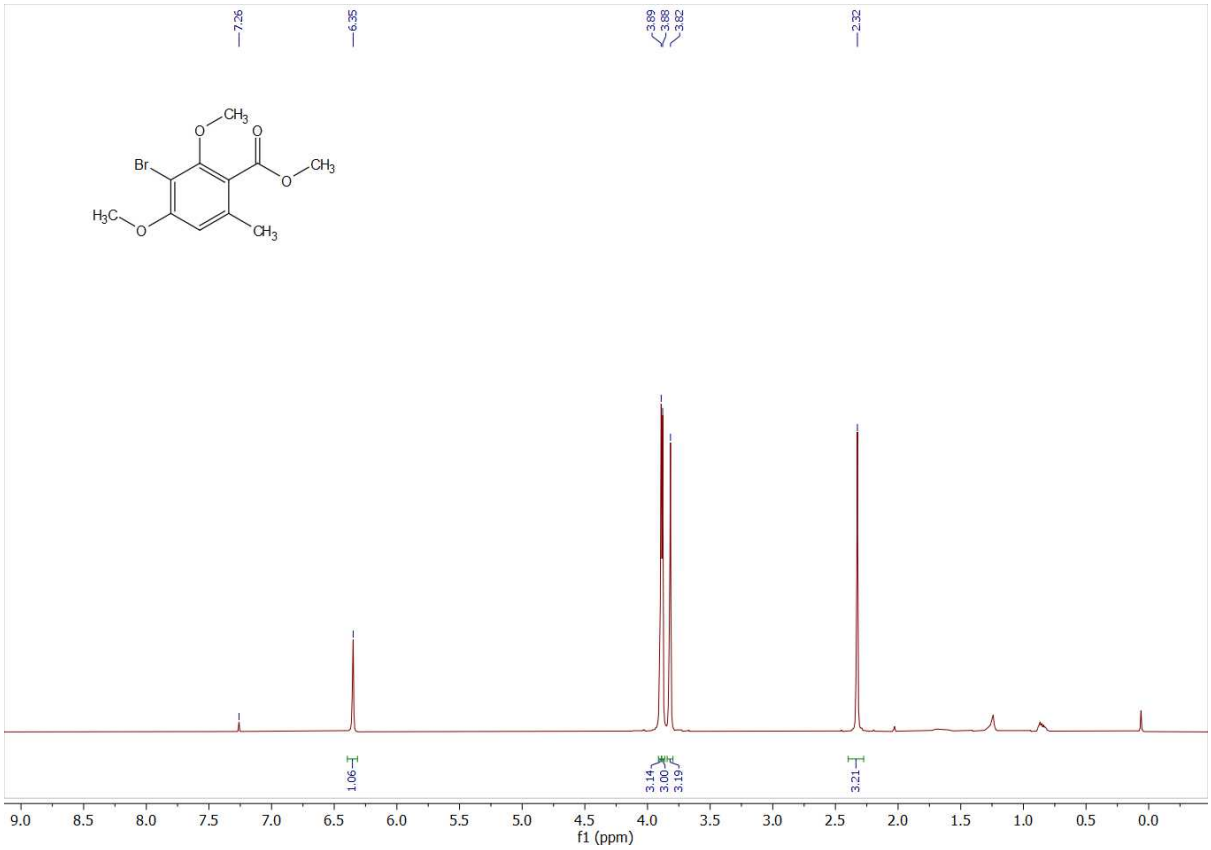
^{13}C{H} NMR of compound 37



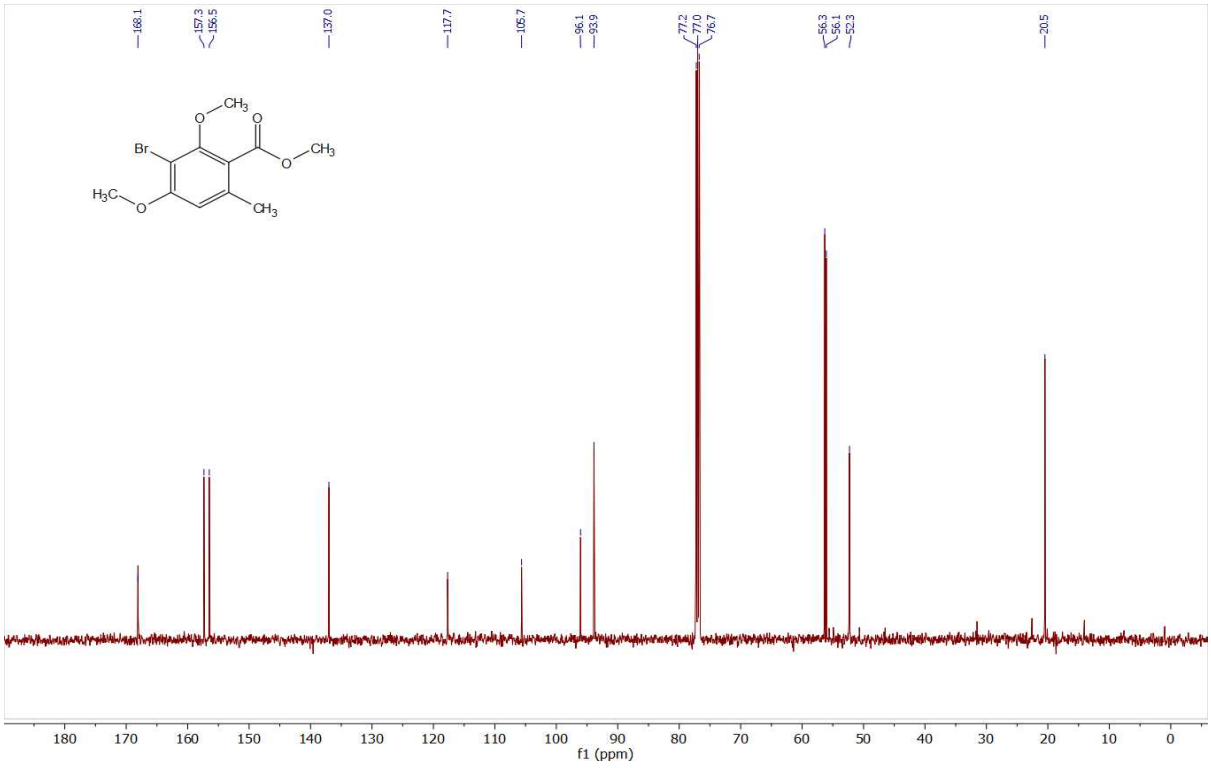
^{1}H NMR of compound 38



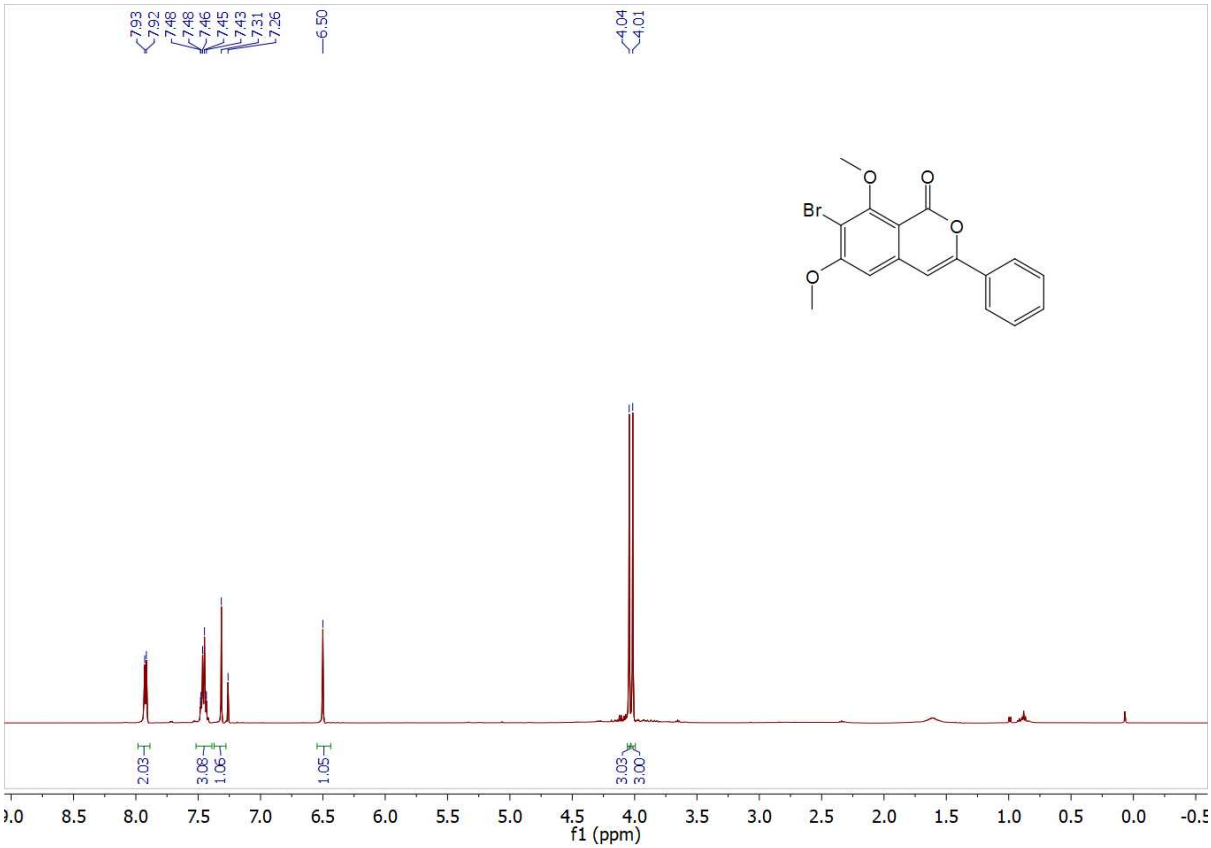
^{13}C{H} NMR of compound 38



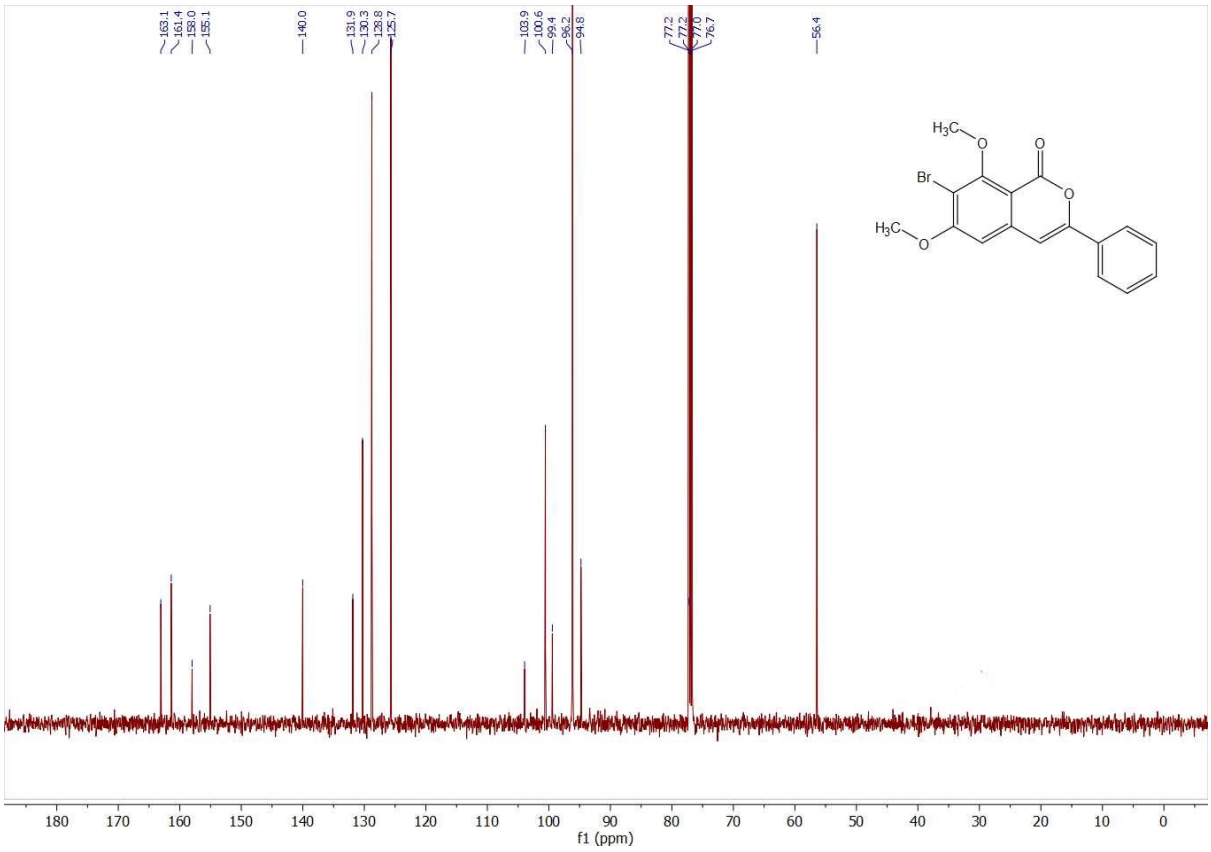
^{1}H NMR of compound 39a



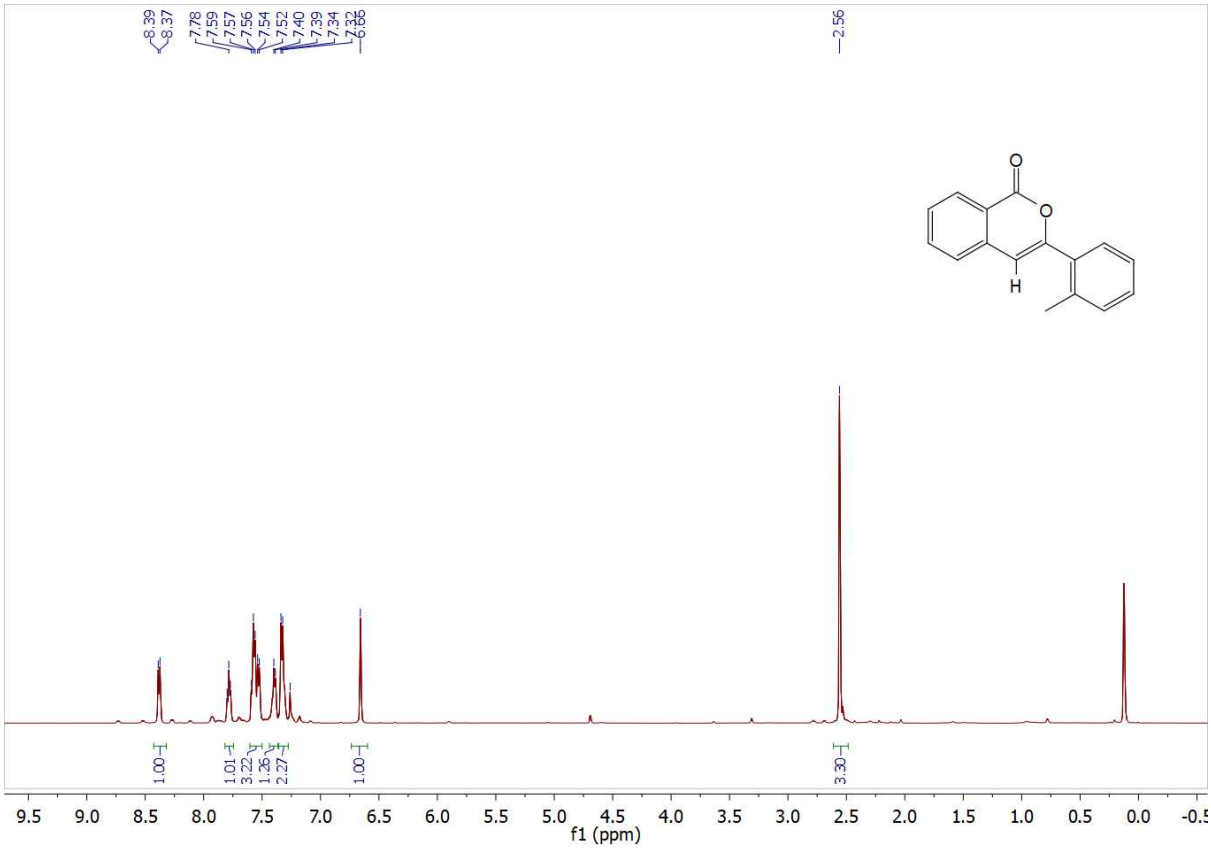
^{13}C{H} NMR of compound 39a



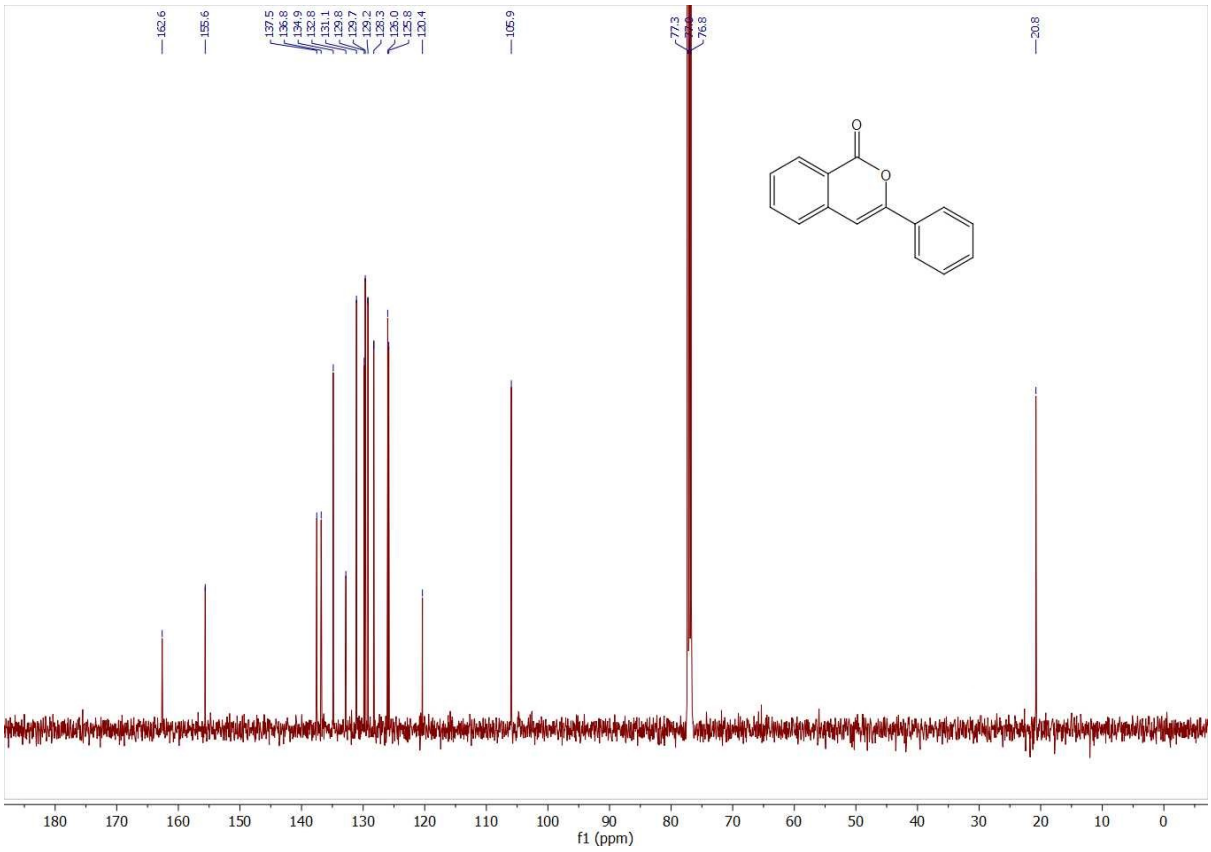
^{1}H NMR of compound 39



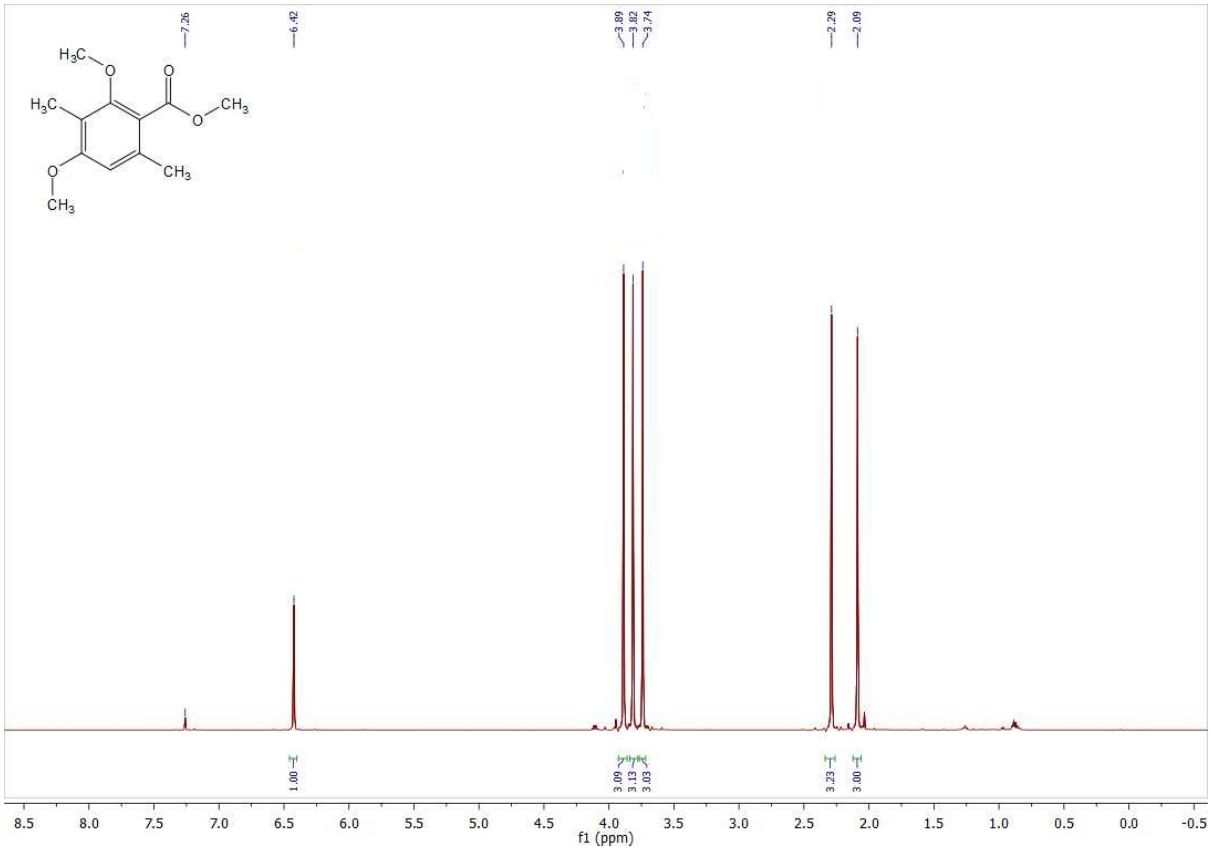
^{13}C{H} NMR of compound 39



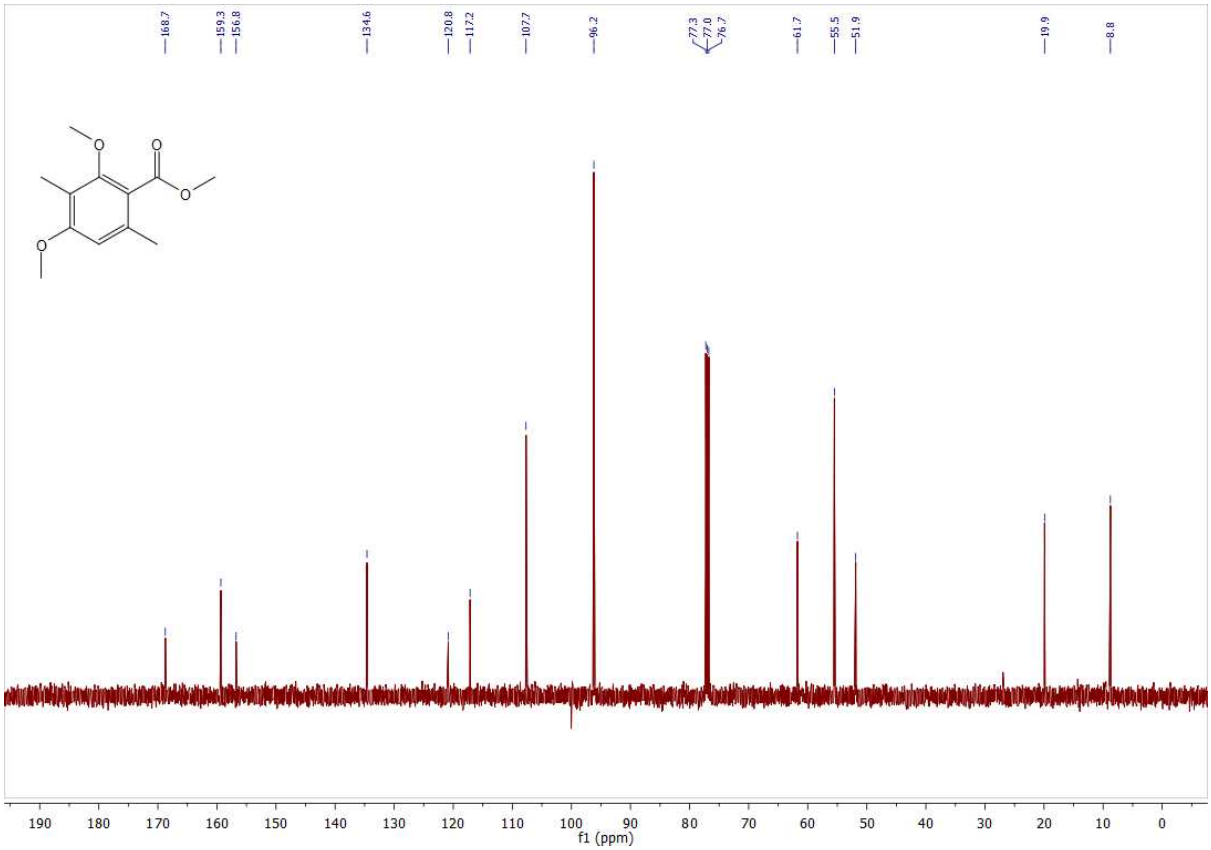
^{1}H NMR of compound 40



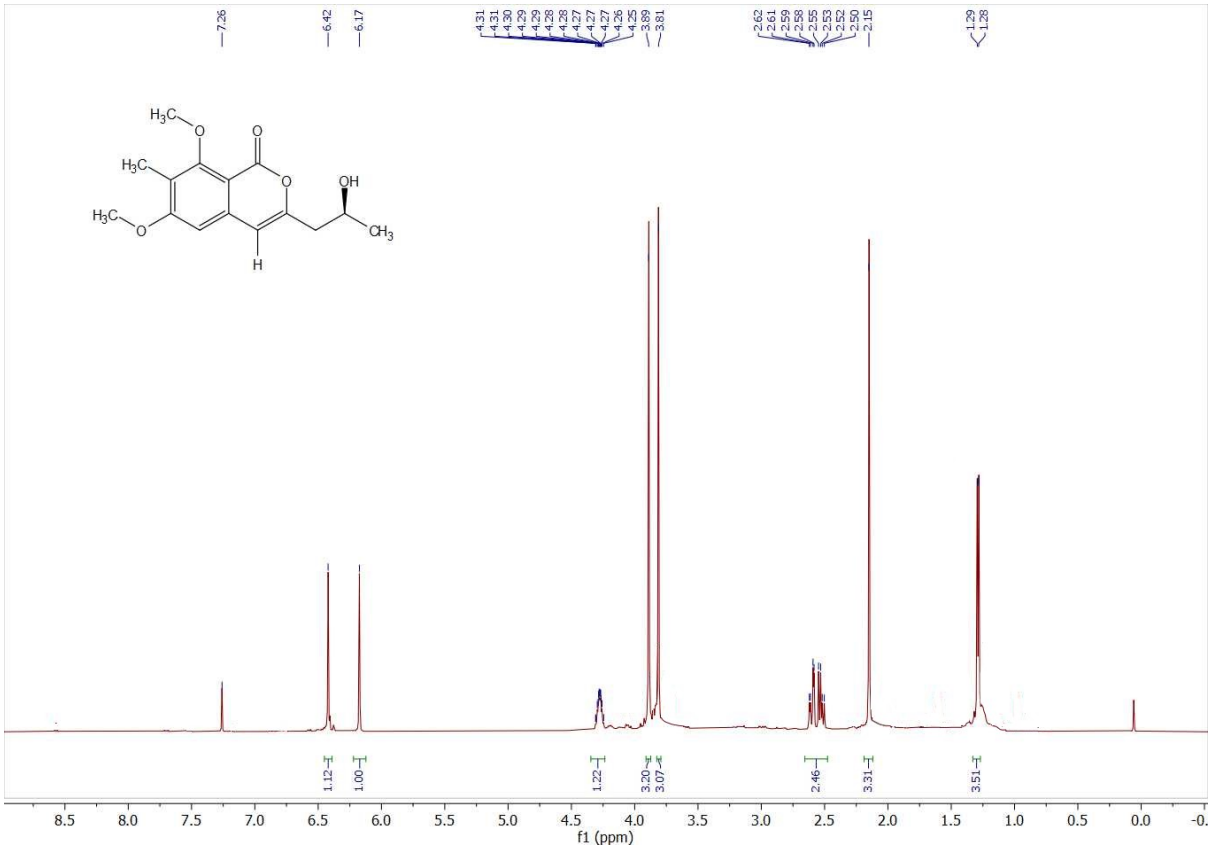
^{13}C{H} NMR of compound 40



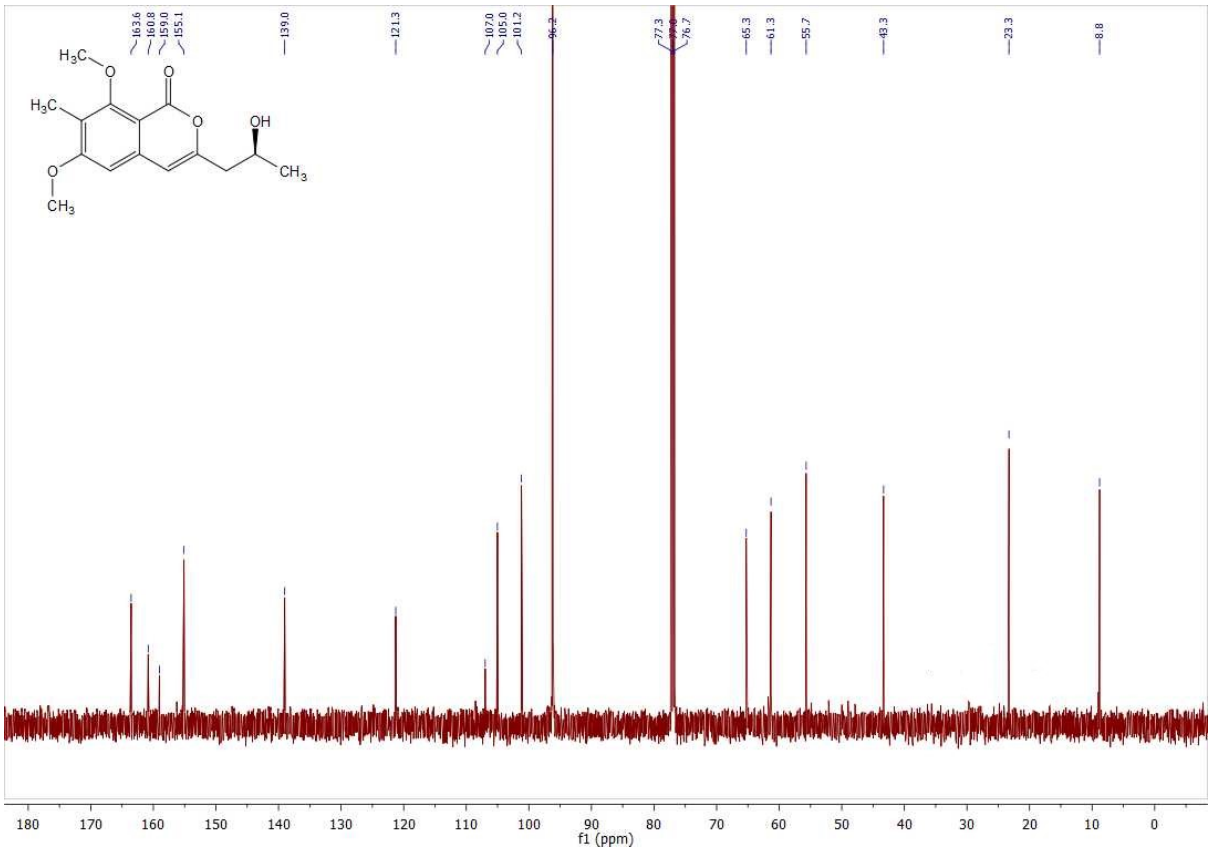
^{1}H NMR of compound 44



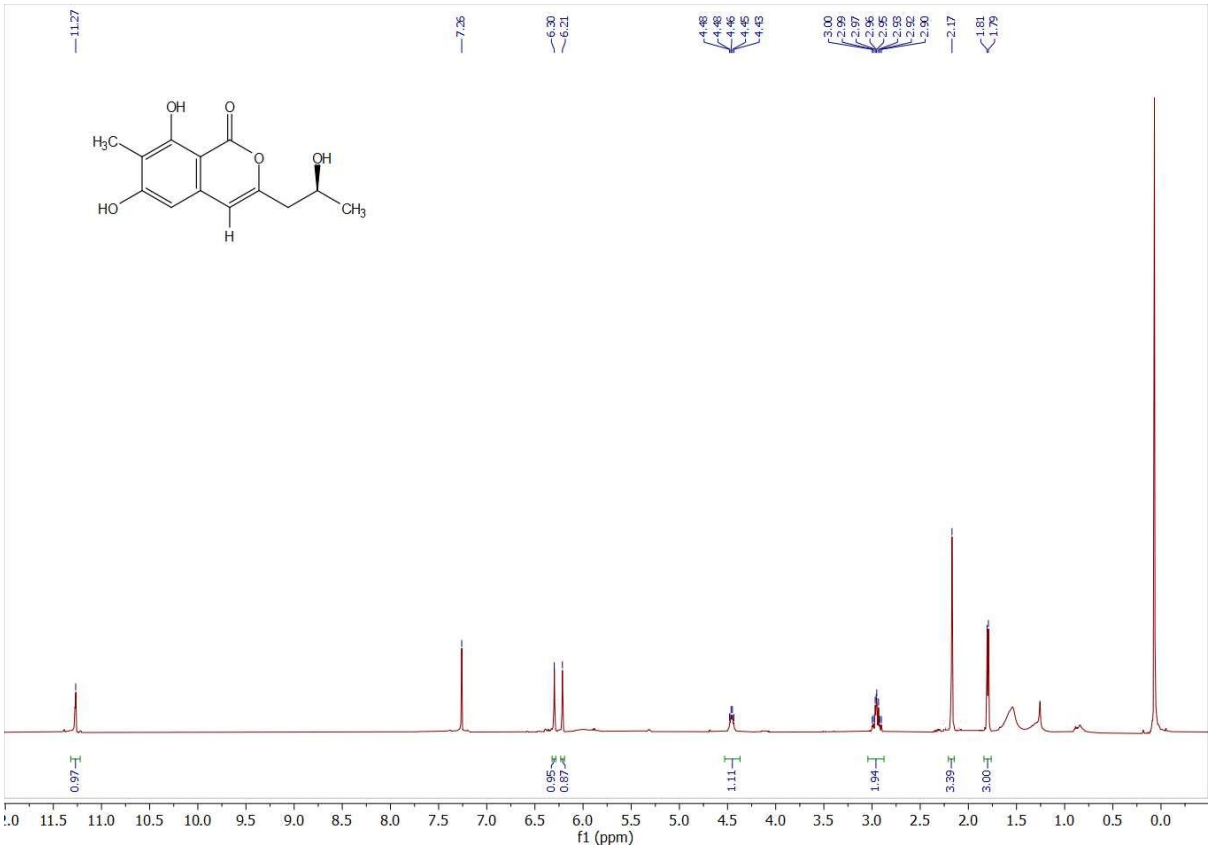
^{13}C{H} NMR of compound 44



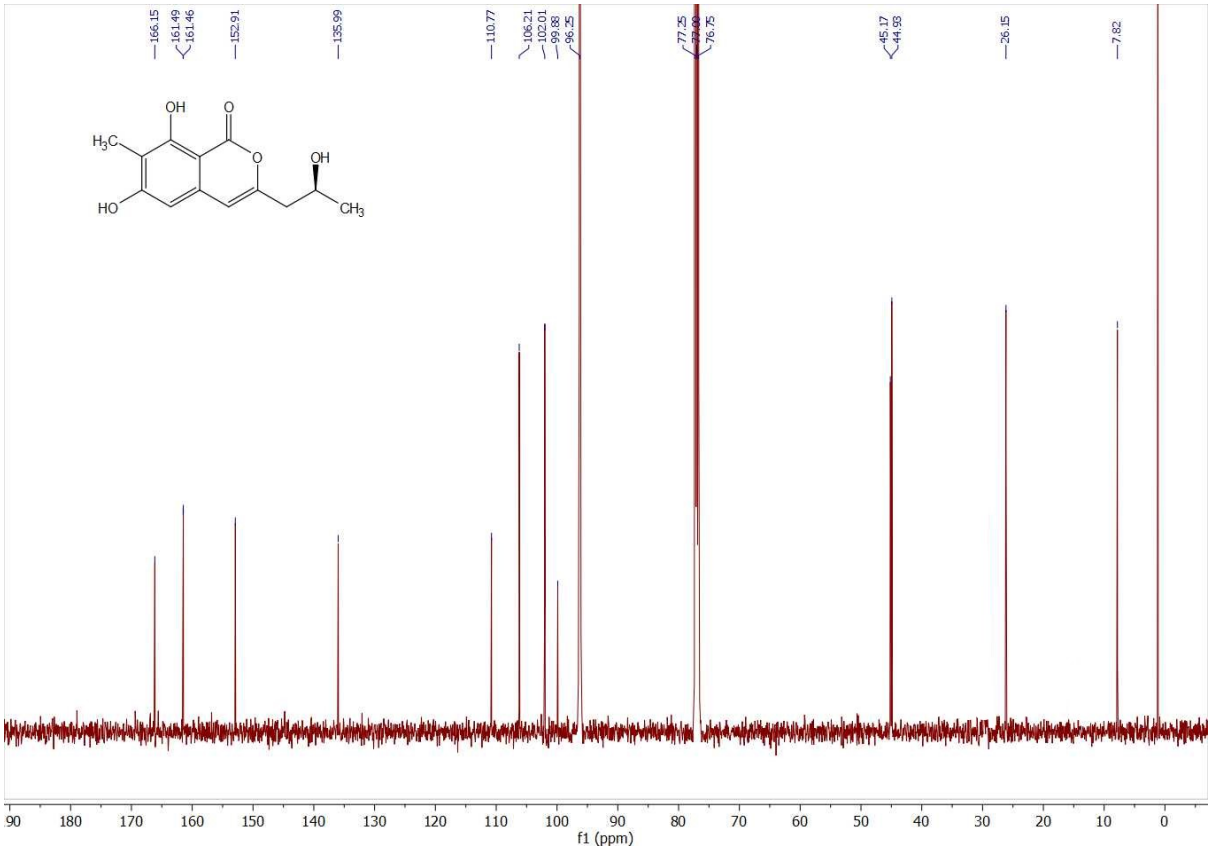
^{1}H NMR of compound 45S



^{13}C{H} NMR of compound 45S



^{1}H NMR of Compound 46S



^{13}C{H} NMR of Compound 46S